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RAPID SEROLOGICAL DIAGNOSIS OF MALARIA: NEED TO INTRODUCE INNOVATIVE TECHNIQUES IN DEVELOPING COUNTRIES

Abdul Gaffar Biloo, Saira Loane

Malaria kills 1-2 million people annually including one million children and infects 300-500 million people worldwide. The disease is present in over 100 countries, threatening 40% of the world population. Malaria is one of the leading causes of morbidity and mortality and is the single largest killer in children aged under five in Africa. It is caused by four species of the Plasmodium (P.) protozoa of which P. falciparum is responsible for most deaths. Reliable diagnosis of malaria requires laboratory confirmation of the presence of malarial parasite in the blood of a febrile child. Traditional methods based on the examination of Giemsa-stained thick and thin blood smears under a microscope, are inappropriate for many areas because there are insufficient microscopes and/or trained microscopists to read and interpret the slides.

Recently, rapid detection methods have been developed for situations where microscopy may not be available. They are based on the detection of antigen released from parasitized red cells. Malaria antigens currently targeted by rapid diagnostic (RDT) are histidine rich proteins II (HRP-II), plasmodium lactate dehydrogenase (pLDH) and plasmodium aldolase. The HRP-II is a water soluble protein produced by asexual stage and young gametocytes of P. falciparum. It is expressed on the RBC membrane and because of its abundance in P. falciparum, it was the first antigen to be used to develop a rapid diagnostic test.

Plasmodium lactate dehydrogenase (pLDH) is an enzyme found in the glycolytic pathway of the malarial parasite and is produced by asexual and sexual stages of the parasite. Different isomers of pLDH for each of the four plasmodia exist and their detection constitutes a second approach to RDT development. Several other enzymes of the malarial parasites involving the glycolytic pathway such as aldolase have also been suggested as a target antigen for RDT for species other than P. falciparum. These new immunochromatographic (ICT) antigen tests are capable of detecting >100 parasites/ul and of giving rapid results in 15 to 20 minutes. They are available commercially in a kit form with all the necessary reagents and the procedure does not require extensive training or equipment to perform or to interpret results. Immunochromatography relies on the migration of liquid across the surface of a nitrocellulose membrane. The tests are based on the capture of parasitic antigen from the peripheral blood using monoclonal antibodies prepared against a malaria antigen target and conjugated to either a liposome containing selenium dye or gold particles in a mobile phase. A second or third capture monoclonal antibody applied to a strip of nitrocellulose acts as the immobile phase. The migration of the antigen-antibody complex in the mobile phase along the strip enables the labeled antigen to be captured by the monoclonal antibody of the immobile phase, thus producing a visible colored line.

The traditional and tedious microscopic examination of blood film carefully by an experienced and trained microscopist of a well prepared and well stained blood films still remains the gold standard for detecting and identifying the malarial parasite, but has undergone very little improvement since its development in the early 1900s. It has the additional advantages of differentiation between falciparum, vivax, ovale and malarial, circulating stages trophozoite, gametocyte, and schizont and determination of level of parasitemia. In inexperienced hands, it can detect 50 parasites/ul (0.001%) of malaria. It is relatively inexpensive, more sensitive and also gives us other information like platelet and leukocyte estimation and the presence of abnormal and immature cells.

The rapid diagnostic tests are simple to use, easy to interpret, produce results in less than 20 minutes, and are as sensitive to microscopy and do not require skilled personnel to perform the tests. They can be used as a supplement in doubtful cases. Studies carried out, locally and internationally, show that results of RDT are comparable to conventional microscopy. A study done in Germany showed a sensitivity of 92.5% and specificity of 98.3% for ICT.
Traditional blood film microscopy for malarial parasite is the gold standard in the presence of experienced microscopist but rapid diagnostic tests can be used as a supplement in doubtful cases. These tests provide an alternative especially in rural areas of developing countries, where microscopy is not available, staff is inexperienced in far flung areas and urgent diagnosis is needed at night, weekend and holidays even in urban areas when available staff is relatively inexperienced.

With the present burden of disease, it is imperative that these rapid and innovative diagnostic tests should be introduced in this scenario and made freely and widely available.

**REFERENCES**


3. WHO. New perspectives: Malaria diagnosis; Approaches to the diagnosis of malaria 2000; WHO/MAL.


ERUPTION TIME OF PERMANENT FIRST MOLARS AND INCISORS AMONG FEMALE PRIMARY SCHOOL CHILDREN OF RIYADH

Arham Nawaz Chohan, Nazeer Bashir Khan *, Lina Al Nahedh **, Mashael Bin Hassan **, Nora Al Sufyani **

ABSTRACT
Objective: To determine the mean eruption time of permanent first molars, central and lateral incisors and to compare the relationship of mean eruption time with body mass index (BMI) in Saudi female primary school children from Riyadh, Saudi Arabia.

Study design: Cross sectional study.

Subjects and methods: The study population comprised of 612 randomly selected primary school children of grade 1 to grade 3. The eruption time of permanent first molars, central and lateral incisors with age, height and weight were recorded.

Results: The mean age of children was 89.3 (SD 9.6) months ranging from 71 months to 109 months. The maxillary right first molar had the lowest mean eruption time of 77.4 (SD 3.9) months and the maxillary right lateral incisor was the last tooth to erupt with eruption time of 98.4 (SD 6.5) months. Furthermore, the mandibular incisors erupted significantly earlier than maxillary incisors. By the age of 100 months, 97% of the girls had all their first permanent molars erupted.

Conclusion: There was no significant correlation observed between eruption times with BMI of the studied teeth except the maxillary right lateral incisor. However, an inverse relationship may exist between the eruption times and BMI. The Saudi female primary school children showed later eruption time of permanent first molars, central and lateral incisors when compared with the reported results of other national studies.

Key words: Eruption time, permanent teeth, Saudi Arabia, female children.

INTRODUCTION

Permanent first molars are the first permanent teeth to erupt in the oral cavity after the age of 5 years. The eruption age of the first permanent molar is one of the milestones by which the normal physical development of the child is evaluated. It has been observed that most of the parents consider tooth eruption as an important event in the child’s development; hence, they often are anxious and concerned about timing and the sequence of eruption. From a clinical aspect, the specific standards on the timing and sequence of emergence of the permanent teeth represent an important resource for general dental practitioners and specialists involved in managing dental problems in growing children.[1] Therefore, the timing and sequence of eruption of permanent teeth are of great significance in children in relation to growth, development and management of dental problems, including the forensic dentistry.[2]

There is no published information available on the eruption time of permanent teeth in all Middle Eastern countries. Therefore, the information utilized in academic and clinical situations on the eruption time of permanent teeth in Middle Eastern countries is still based on other populations.[3,4] Several studies were conducted from the middle of twentieth century in different populations on the eruption times of permanent teeth. These studies permanent teeth, and this may be attributed to racial
showed that variation exists in the eruption times of differences⁵. It has also reported that some other variables like genetic and hormonal factors, geographical, tribal, gender, as well as economic status, nutrition and growth parameters have been shown to exert an influence on eruption timing and emergence⁶. Few studies have also reported a relationship between the eruption time, with the weight and height of children: children who are below average weight and height showed a later eruption time than those children who are within the standard range⁷. A recent study reported eruption times of primary dentition in Saudi children¹¹ and eruption time of permanent first molars and incisors in Saudi male primary school children¹². However, there is no such information available on the eruption times of permanent teeth in Saudi female children. Therefore, the objectives of the present study were to determine the mean eruption time of permanent first molars, central and lateral incisors and to compare the relationship of mean eruption time with BMI in Saudi female primary school children from Riyadh, Saudi Arabia.

SUBJECTS AND METHOD

The population used for this cross-sectional study conducted from November to December 2004, corresponding Shawwal 1425 Hijri, comprised of students of grade 1 (G1) to grade 3 (G3) from female primary school children of Riyadh. Three primary schools were randomly selected from different regions of Riyadh by the list of schools provided by the Ministry of Education. In addition, a private school was also randomly selected to ensure representation from all segments of the society. Prior to the commencement of the study, permission was taken from Ministry of Education, Riyadh. Letters were sent to respective heads of the schools stating the aims and objectives of the study. All the children of G1 to G3 from the selected schools were screened and the children who fulfilled the inclusion criteria were selected for further examination. A total of 1300 children were examined and only 612 children were found suitable for the study. The data were collected over a period of one calendar month. All selected children in the sample were healthy and they satisfied the criteria of at least one tooth that had just erupted.

The criterion for a just erupted tooth was defined as; a tooth deemed to have emerged if any part of it (tip of incisal edge or one cusp of molar) was visible in the mouth¹³. The calibration of the examiners was carried out by showing them the clinical pictures of just erupted teeth.

The dental examination was carried out by two authors (LN and NS) using a wooden spatula to retract soft tissue and then by direct visual inspection. The status of eruption of permanent tooth was recorded. In some cases disposable mirror was also used to confirm the eruption status. The selected children were then sent to third author (MHi) to record the weight and height. Students were weighed in kilograms using a commercial digital scale after removal of the shoes only. The height of the children was measured using a wall-mounted ruler on the child's head with their back and knees completely straight, and their feet together. The height was then rounded to the nearest centimeter. The demographic information about the children such as age, educational level, date of birth, place of birth, and family name was recorded on the form, taken from children's personal data files of the school. The data were then entered into the computer utilizing the Statistical Package of Social Science (SPSS) program version 10. Descriptive statistics (minimum, maximum, mean, standard deviation, median and range [R]) of eruption time was computed for each tooth. Different percentiles (P3, P10, P25, P75, P90 and P97) of the time of eruption of permanent teeth were also calculated. Body mass index was calculated using the following formula:

\[
BMI = \frac{\text{Weight (kg)}}{\text{Height(m)}}^2
\]

Independent-sample t-test was used to find any significant difference in the mean eruption time of right and left side, and also upper with lower teeth. Pearson correlation was utilized to find the correlation between eruption time and BMI.

RESULTS

The mean age of 612 children was 89.3 (SD 9.6) months ranging from 71 months to 109 months. Table 1 shows

<table>
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<th>Tooth</th>
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the descriptive statistics (minimum, maximum, mean, standard deviation, median and range [R]) of eruption time of permanent first molars, central and lateral incisors. The mean BMI was 15.8 (± 2.6) kg/m². The maxillary right first molar (#16) had the lowest eruption time of 77.4 ± 3.9 (R: 71-84) months and maxillary left first molar (#26) had second lowest mean value of 78.7 ± 5.3 (R: 71-88) months. The difference of these two means was only 1.3 months. However, the difference of median values of eruption time of these two molars was 2 months. The mandibular central incisors (#31, #41) succeeded the maxillary first molars with mean values of 82.6 ± 7.7 (R: 71-103) and 82.6 ± 8.2 (R: 72-103) months, and the left and right mandibular first molars closely followed with mean values of 83.4 ± 6.9 (R: 71-96) months and 84.0 ± 7.6 (R: 71-101) months respectively. The left and right maxillary lateral incisors were the last teeth to be erupted in our sample with mean values of 96.0 ± 5.7 (R: 76-104) months and 98.4 ± 6.5 (R: 77-109) months respectively. There was statistically significant difference between the mean eruption times of maxillary and mandibular permanent first molars, central and lateral incisors (p < 0.05). However, there was no significant difference observed between the mean eruption times of right and left sides (p > 0.05).

The minimum range of variation of eruption (13 months) was seen in the permanent maxillary right molar (tooth #16); the maximum range of variation was seen in permanent maxillary right lateral incisors (37 months) as shown in Table 1. Table 2 shows different percentiles 3rd, 10th, 25th, 75th, 90th and 97th for eruption time (months) for girls.

Table 2: Percentiles (3rd, 10th, 25th, 75th, 90th and 97th) for eruption time (months) for girls

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The age of 100 months 97% of the girls had their four permanent first molars (#16, #26, #36, #46) erupted. In addition, the four permanent central incisors erupted between the ages of 72 and 103 months in 94% of the girls. The correlation of BMI and the eruption times is illustrated in Table 3. There was no statistically significant correlation between these two features except for tooth #12. However, there were more negative correlations than positive ones, which show that there may be an inverse relationship between eruption time and BMI. Comparison of mean eruption time of permanent first molars and incisors of the present study with male Saudi primary school children is shown in Table 4. The data of mean eruption time of Saudi male children was taken from the authors' earlier publication. There was no significant difference between the mean eruption time...
between male and female children.

**DISCUSSION**

Several reported studies have targeted different populations to determine the mean eruption times of the permanent teeth. However, until the near past, there was no reported data available on eruption times of permanent teeth for Saudi children. Due to this reason, the standards for eruption times of permanent teeth were based on non-Saudi populations. The documented variation in eruption time values in different populations makes it necessary to investigate the normal values of eruption times for Saudi children. Recently a study was conducted on eruption time of permanent first molars and incisors teeth in Saudi male primary school children. The present study provides the basic information on the mean eruption time of permanent first molars, central and lateral incisors in Saudi female primary school children of G1 to G3 aged between 71 to 109 months.

The results of the study showed that the difference in the mean eruption time of permanent first molars and incisors (central and lateral) was statistically significant for both the jaws. It was observed that the mandibular central and lateral incisor teeth have an earlier eruption time than the maxillary counterparts. These results are in agreement with several other similar studies carried out in various countries. However, an opposite pattern of eruption time was observed in case of permanent first molars, which is not in agreement with most of the reported studies. Table 5 illustrates the comparison of mean eruption time of permanent first molars and incisors of present study with Ghana, Nigeria, Iran, Japan, Australia, and USA. Saudi female children showed later eruption than all other countries, except Iranian females. When comparing the eruption time difference between the right and left sides, the greatest temporal difference was seen in maxillary lateral incisors, which was about 2.4 months, followed by maxillary first molars with a time difference of 1.3 months, and the difference was not statistically significant. Stewart et al. have reported that these time differences are not systematic, and can be of any length between 2 months to 2 years. Recent studies show a very high caries prevalence among Saudi preschool and primary school children in Riyadh. Prevalence of caries affects the emergence time of permanent teeth due to premature loss of their predecessors. This hypothesis is supported by another study which reported that premature extraction of deciduous teeth does not advance the emergence of their successors. Since the caries severity in Saudi school children has increased in the last decade, probably this factor may contribute to the observed advancement in tooth emergence.

The results of the present study did not reveal any significant correlation between BMI and eruption time except for maxillary right lateral incisor (#12). However, more negative correlations than positive indicate an inverse relationship between BMI and eruption time. This finding is in agreement with Nishwander and Sujaku study, who have reported that a trend was observed of general advancement in physical development with early eruption.

Similarly, Hoffding et al. reported that only minor changes in tooth emergence was observed with pronounced acceleration in physical development.

Considering the permanent first molars, central and lateral incisors of these Saudi children, the mean eruption time was later than that reported in children from Ghana, Nigeria, Iran, Japan, and similarly, USA and Australian children had earlier eruption time than Saudi children except for maxillary lateral incisors. However, Saudi children exhibited earlier eruption time than the Iranian children except for mandibular molars and central incisors. When comparing the mean eruption times of permanent first molars and incisors between male and female Saudi children, no statistically significant difference was observed except for mandibular right first molar (#46). Several studies in various populations have thought that factors like nutrition, socio-economic status, genetics and geographic location could have an influence on the emergence time of teeth. Clemens et al. claimed that mean emergence time was earlier in the children with higher socio-economic status.
The study was limited to the female primary school children, as it was conducted by the female dentists in all-female schools only due to socio-religious norms of Saudi Arabia. Nevertheless, the study has provided useful information about the eruption time in permanent teeth in Saudi female primary school children of G1 to G3 of Riyadh, Saudi Arabia.

CONCLUSIONS

The mandibular central and lateral incisors teeth erupted before the maxillary counterparts and reverse trend were observed in permanent first molars. The mean eruption time of Saudi children was later than most of the reported populations. There may be an inverse relationship between BMI and eruption time.

REFERENCES


ORIGINAL ARTICLE

AWARENESS ABOUT REPRODUCTIVE HEALTH AND RIGHTS AMONG STUDENTS OF A PUBLIC UNIVERSITY IN KARACHI, PAKISTAN: A CROSS SECTIONAL STUDY

Naheed Nabi, Waris Qidwai, Farhat Batool*, Syed Iqbal Azam**

OBJECTIVE

Objective: To determine the knowledge, attitude and practices of Karachi University students about reproductive health and rights.
Design: Cross sectional study
Methods: A survey was conducted from February to May 2005 to determine the understanding and knowledge related to reproductive health and rights among the students of the department of Biochemistry, University of Karachi, Pakistan. A pre-coded questionnaire was developed and pre-tested. The questionnaire was introduced to those students, who agreed to participate in the study. Data collected was double entered and analyzed on SPSS and Epi-info latest version.
Results: Fifty five percent (55%) of participants believed the reproductive rights to be as important as other human rights. About 80% of participants thought that proper birth spacing can improve maternal and child health but very few Pakistani women have birth spacing rights. Quality of life of women and men can be improved by knowing their reproductive rights in view of 71% and 63% of respondents respectively.
Conclusion: Although one third of participants claimed to be aware of their reproductive rights but majority were unable to identify what exactly comes under the domain of reproductive rights. Majority knew that appropriate use of contraception and birth spacing can have positive impact on maternal and child health. The study recommends that awareness sessions should be conducted at all levels of society and more efforts should be made to improve reproductive health and increase awareness and the implementation of reproductive rights.

Key words: Reproductive health, Reproductive rights, Knowledge, Attitude, Practices

INTRODUCTION

Reproductive health is a “state of physical, mental, and social well-being in all matters relating to the reproductive system at all stages of life”. Reproductive health therefore involves the capability and freedom of reproduction, safe and satisfactory sex life. It’s the right of every man and woman to have access to safe, cost effective, acceptable and successful methods of contraception of their choice. Availability of proper health care services can facilitate the safe outcome of pregnancy and childbirth. Reproductive health care is defined as the “constellation of methods, techniques and services that contribute to reproductive health and well being by preventing and solving reproductive health problems”. Sexual health covers not only the reproduction and control of sexually transmitted diseases through counseling and care but is also helpful in enhancement of life and personal relations.

The reproductive rights are the “major rights of the married couple and individual to decide, in a free and responsible manner, the number of children, the place and time of childbirth, to make use of the relevant information and means to regulate fertility as well as the accessibility of high standards of sexual and reproductive health”. A very large number of mothers and children die and suffer every year in pregnancy, childbirth and early childhood. Majority of deaths and physical and psychological pain and distress occur in low and middle income countries. Nearly 30,000 children die every day and 10.6 million children die each year. More than 70%
of all child deaths occur because of preventable and treatable conditions. More than half of all childhood deaths are contributed by malnutrition, although it is rarely mention as a direct cause.2

Every year 52,900 mothers die mostly from avoidable causes.3 Over 300 million women experience short or long term illness related to pregnancy and child birth in the developing world currently.4

Main factors responsible for 70% of all maternal deaths are hemorrhage (25%), infection (15%), unsafe abortion (13%), high blood pressure (12%), and obstructed labor (8%). Women from poor household, with a daily income of less than US $1, are at least 300 times more likely to die due to pregnancy-related causes as compared to the well-to-do women, all over the world. World is highest rates of unplanned pregnancies, maternal deaths, unsafe abortions, child marriages, sexual trafficking and violence and increasing numbers of HIV/AIDS infections are seen in South Asian women.5

Maternal mortality in South-East Asia accounts for about 40% of global deaths. Over 50 per cent of infant deaths in South – East Asia occur during the neonatal period, nearly two-thirds within the first week of birth, mostly due to perinatal causes.5

Three women die every hour of unsafe and often illegal abortions in South Asia. In Sri Lanka, a leading cause of maternal mortality is unsafe abortion. Most abortions in Bangladesh are illegal and 22 women are hospitalized every day for abortion related complications. Over half of all girls are married by age of 18 in India, Nepal and Bangladesh. Although child marriage is illegal in all three countries, but huge number of children are married every year.6

Higher numbers of maternal deaths in the world are a growing problem especially in India with highest reported maternal deaths6 and also in Pakistan with MMR of 340 per 100,000 live births.6 Awareness and practices regarding reproductive health and rights are in a poor state in Pakistan with contraceptive prevalence of 12% in 1990-91 and 24% in 1996-97.7 The situation about safe sex is unclear. HIV prevalence in Pakistan for adults aged 15-49 was reported to be very low i.e. 0.11% in 2004 and 2005.8 However figures for other STDs may be much higher. In Pakistan, family planning rate has improved from 9.15% in 1996 to 24% in 1997, 31% in 2002,9 and 34% in 2005.10 Still Pakistan is much behind in the region as compared to contraceptive prevalence rates currently 54% in Bangladesh, 71% in Sri Lanka and 48% in India.10 Information to get needed insight into the specific needs of the younger generation on issues related to practices of reproductive health and rights.10

We therefore planned a study to determine the knowledge, attitude and practices of University students about reproductive health and rights in Karachi, Pakistan.

SUBJECTS AND METHODS

A cross sectional study was conducted from February to May 2005 amongst the students of the Department of Biochemistry, University of Karachi.

After extensive literature search and discussions, a questionnaire was developed to document the awareness about reproductive health and rights among university students. It was pre-tested before the final administration on students in the department of Pharmacy, Karachi University. After explaining the study objectives in detail, verbal informed consent was taken from those who agreed to participate in the study. Assurance with regards to confidentiality of information was provided to study participants.

The questionnaire was handed out to consenting students. They returned the completed forms to the study investigators. Out of the total of 125 students the department, one hundred and fifteen students returned the filled questionnaire and ten refused to participate in the study. Epi-info and SPSS software were used for data management and analysis respectively. Frequencies of all variables in the study and mean with standard deviation of age were calculated.

RESULTS

Out of the total of one hundred and fifteen students, majority were females (72%) and Urdu speaking (63%). Ages of the respondents were ranging between 18 to 25 years. Similarly majority of the respondents were either Honors' (49%) or Masters' (45%) students. Access to television was common and two third of them were having cable connection. (Table 1)
Reproductive health and rights awareness

Table 1: Socio-Demographic profile of respondents (n=115)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (± Standard Deviation)</td>
<td>21.2 (±1.3)</td>
<td></td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td>Female</td>
<td>83</td>
<td>72</td>
</tr>
<tr>
<td>University Class:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bachelor</td>
<td>04</td>
<td>03</td>
</tr>
<tr>
<td>Honors</td>
<td>56</td>
<td>49</td>
</tr>
<tr>
<td>Masters</td>
<td>52</td>
<td>45</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>Ethnicity:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urdu speaking</td>
<td>72</td>
<td>63</td>
</tr>
<tr>
<td>Punjabi</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Sindhi</td>
<td>05</td>
<td>04</td>
</tr>
<tr>
<td>Pashto</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>Balochi</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Sonathan</td>
<td>06</td>
<td>05</td>
</tr>
<tr>
<td>Not disclosed</td>
<td>04</td>
<td>03</td>
</tr>
<tr>
<td>Access to television at home</td>
<td>105</td>
<td>91</td>
</tr>
<tr>
<td>Access to cable television at home</td>
<td>69</td>
<td>60</td>
</tr>
<tr>
<td>Watch TV programs that address social issues</td>
<td>75</td>
<td>66</td>
</tr>
<tr>
<td>Watch TV programs that address health issues</td>
<td>93</td>
<td>81</td>
</tr>
</tbody>
</table>

According to the student’s opinion, more than half of them thought that reproductive rights have similar importance as other human rights. Reported awareness about reproductive rights is although low but higher in urban population as compared to rural population. Majority of them thought that poverty alleviation, knowing the reproductive rights and reduction in verbal abuse can lead to better quality of life (Table 2A).

Table 2-A: Student views on reproductive rights (n = 115)

<table>
<thead>
<tr>
<th>Student’s View</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive rights are as important as other human rights?</td>
<td>63</td>
<td>55</td>
</tr>
<tr>
<td>Reproductive rights awareness in Pakistan?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban women</td>
<td>45</td>
<td>39</td>
</tr>
<tr>
<td>Rural women</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Urban man</td>
<td>40</td>
<td>35</td>
</tr>
<tr>
<td>Rural man</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>Reproductive health issues as part of National Health Issue</td>
<td>87</td>
<td>76</td>
</tr>
<tr>
<td>Does verbal abuse exist in Pakistan?</td>
<td>78</td>
<td>68</td>
</tr>
<tr>
<td>Does it affect reproductive rights?</td>
<td>45</td>
<td>39</td>
</tr>
<tr>
<td>Poverty reduction can improve reproductive rights?</td>
<td>84</td>
<td>73</td>
</tr>
<tr>
<td>Understanding and practice of reproductive rights is related to education?</td>
<td>84</td>
<td>73</td>
</tr>
<tr>
<td>Reproductive rights related to overall health?</td>
<td>94</td>
<td>82</td>
</tr>
<tr>
<td>Threat to reproductive rights of working women at work in Pakistan</td>
<td>33</td>
<td>29</td>
</tr>
</tbody>
</table>

About one third of the students thought that women in Pakistan have birth spacing rights. Majority of them thought that proper birth spacing, knowledge and practices of family planning can improve maternal and child health. In view of about two third of the respondents early detection and management of STI’s can improve reproductive health. (Table 2B)

Table 2-B: Student views on reproductive rights (n=115)

<table>
<thead>
<tr>
<th>Student’s View</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women in Pakistan have birth spacing rights?</td>
<td>39</td>
<td>34</td>
</tr>
<tr>
<td>Proper birth spacing can improve maternal and child health?</td>
<td>92</td>
<td>80</td>
</tr>
<tr>
<td>Awareness about family planning among Pakistani youth can improve reproductive rights situation?</td>
<td>87</td>
<td>76</td>
</tr>
<tr>
<td>Proper family planning practices can reduce maternal mortality in Pakistan?</td>
<td>82</td>
<td>71</td>
</tr>
<tr>
<td>High maternal and child mortality reflects poor reproductive health?</td>
<td>67</td>
<td>58</td>
</tr>
<tr>
<td>Is there a relationship/link between sexuality and gender</td>
<td>60</td>
<td>52</td>
</tr>
<tr>
<td>Decision making about induced abortion should be the right of;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Student's View</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Male partner</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Both</td>
<td>55</td>
<td>67</td>
</tr>
<tr>
<td>Doctor</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Improved maternal health reflects improve reproductive rights</td>
<td>78</td>
<td>68</td>
</tr>
<tr>
<td>Demand for safe sex is the right of:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>04</td>
<td>03</td>
</tr>
<tr>
<td>Woman</td>
<td>05</td>
<td>03</td>
</tr>
<tr>
<td>Both</td>
<td>88</td>
<td>76</td>
</tr>
<tr>
<td>Knowledge of safe sexual practices can help in prevention of sexually transmitted infections</td>
<td>82</td>
<td>71</td>
</tr>
<tr>
<td>Early detection and treatment of sexually transmitted infections can improve reproductive health</td>
<td>73</td>
<td>63</td>
</tr>
<tr>
<td>Reproductive rights should be observed in context of:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religion</td>
<td>47</td>
<td>46</td>
</tr>
<tr>
<td>Human Rights</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Both</td>
<td>42</td>
<td>41</td>
</tr>
<tr>
<td>None</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Is there a relationship/ link between sexuality and health?</td>
<td>73</td>
<td>63</td>
</tr>
</tbody>
</table>

**DISCUSSION:**

Reproductive health and reproductive rights have been emphasized more in the past two decades as main health issues for the well-being of human and encompass a broad list of issues. According to the Ministry of Health, Pakistan has 12.5% burden of diseases related to reproductive health. Ministry of Health of Pakistan has set reproductive health goals to be achieved by the year 2015. These goals are to decrease the infant mortality rate from 103 to 40, maternal mortality ratio from 340 to 140, increase births by skilled attendants from 24% to 90% and contraceptive prevalence rate to increase from 34 to 55%\(^1\). Currently improvement in these goals is very slow and vary in numbers for different goals and far behind from the targeted goals for year 2015\(^2\). In urban slums, majority of women consult LHVs for reproductive health care mainly because they are females and perceived to be very expert in dealing these issues\(^3\).

This study population was an educated young population. It was expected that they will have better knowledge as compared to general population about issues related to reproductive health and their rights. In the opinion of more than half of the respondents’ quality of life of women and men can be improved by being aware of their reproductive rights and they can handle reproductive health issues more confidently. Similarly, majority of them thought that appropriate birth spacing should improve maternal and child health. In fact, regardless of educational level about 40% of the births in Pakistan are less than two years apart\(^4\). Urban women had shorter birth spacing than rural women, and educated females achieve their family size more rapidly and with high parity (4+) have longer intervals due to contraception. In the urban areas of Punjab and Sindh, longer birth spacing was recorded than in the rural areas\(^5\). In Pakistan contraceptive prevalence rate is only 34%\(^6\), although about two third of study participants thought that proper contraceptive practices can reduce maternal mortality.

A little more than a third of the respondents listed the type of issues related to reproductive health. Major reproductive health issues like maternal and child health, HIV/AIDS was mentioned only by 6.8% and 4.5% respondents respectively. Similarly other important reproductive health issues like sexually transmitted diseases, abortions, short birth spacing, divorce, and sexual, mental and physical abuse were not mentioned by the respondents although they identified unprotected sex as a reproductive health issue. Similar pattern in terms of reproductive rights especially divorce was observed among Egyptian women that they did not consider it as their reproductive right because of its consequences on social acceptance and support although it is legally and religiously allowed\(^7\). The lack of knowledge of study subjects shows that literacy itself does not affect the knowledge about reproductive health and rights. Similarly, majority of the respondents were of the view that reproductive rights should be observed in relation to either religion or religion and human rights both but in practice other factors such as cultural, social and perhaps religious practices could be the important contributors.

In the opinion of the respondents, awareness about reproductive rights although low but is slightly higher in urban population as compared to rural population. Similarly it is low among females as compared to males. It might be due to the low social status of women, the historical gender bias against women, their lack of decision-making power in the family, poverty, ignorance, illiteracy and malnutrition, unequal access to resources, and, in some settings, harmful traditional practices affect the women in achieving their reproductive health and rights\(^8\).

About half of our study participants were not aware of the fact that high maternal and infant mortality reflects poor reproductive health which is a major health concern in Pakistan.
According to most of our study participants, safe sex should be the right of both partners which can help in preventing sexually transmitted diseases; however in our cultural setting it is mostly the choice of the male partner. A link between sexuality and health were identified by most of the study participants.

Induction of abortion should be the right of both partners according to most of the study participants. In Pakistan data collection about induction of abortion is difficult because of social, legal, cultural and religious constraints. In contrast to these constraints, most of the abortions are conducted by traditional birth attendants and 23% end up in hospitalization for complications. Estimated abortion rate is 29 per 1,000 women. Generally, it is thought that decision about induction is taken mostly either by husband or by other family members.

Most of the respondents thought that verbal abuse exist in Pakistan and it affects the reproductive rights. Awareness sessions should be planned through social and religious motivators. Reproductive right and health should also be the part of curriculum not only in professional colleges, universities but also at least at higher secondary levels keeping in view the sensitivity of subject at different levels.

More efforts should be made for activities such as antenatal care, child and mother nutrition, enhanced family planning practices, safe delivery methods and prevention of sexually transmitted infections which are the key reproductive health issues in order to reduce future morbidity and mortality.

More such studies should be carried out in different segments of population in Pakistan as the current study only covers a segment of the population.

**CONCLUSION**

In this study, the reproductive rights were identified as important as other human rights by the university students but there is a need to improve the awareness about it.

Reproductive health can be improved by alleviating poverty, improving health care system and educating women about birth spacing, importance of antenatal care, safe sex, and complications related to induction of abortion, proper family planning practices and identification and management of sexually transmitted infections.

**REFERENCES**


13. Summary of project, Promoting Interventions for safe motherhood (PRISM) PAK/01/P01-01/P01.


ORIGINAL ARTICLE

CORRELATION OF ADJUSTED BLOOD REQUIREMENT INDEX WITH TREATMENT INTERVENTION AND OUTCOME IN PATIENTS PRESENTING WITH ACUTE VARICEAL BLEEDING

Bader Faiyaz Zuberi, Masooda Fatima Riaz, Binish Arif Sultan, Parkash Gobindram, Asma Farooq, Rashid Qadeer, Abdul Rauf Memon, Salahuddin Afsar

ABSTRACT
Objective: To determine the correlation of ABRI with treatment intervention and outcome as discharged or expired in patients of acute variceal bleed.
Design: Cross-sectional study
Patients and Methods: Records of all the patients admitted in Medical Unit-IV, Civil Hospital Karachi with acute variceal bleeding during January 2004 to October 2006 were retrieved. Use of vasoactive agents (Terlipressin/Octreotide), endoscopic band ligation (EBL) and outcome (Discharged/Expired) were noted. ABRI was calculated by the following formula:

\[ ABRI = \frac{\text{Blood Units Transfused}}{[\text{Final Hematocrit} - \text{Initial Hematocrit}] + 0.01} \]

Mean ABRI were compared by Student’s ‘t’ test according to vasoactive therapy, EBL and outcome.
Correlation of ABRI with the same variables was also studied by plotting Receiver Operative Curves (ROC).
Results: Seventy six patients fulfilling inclusion criteria were selected. No statistically significant difference was observed in the mean ABRI scores when compared according to vasoactive drug administration, EBL and outcome. Significant correlation with mortality was seen on ROC plot with significantly larger area under the curve.
Conclusion: ABRI correlated significantly with mortality in this study. Larger prospective studies with appropriate power are required to evaluate its association with other variables.
Key Words:
Varices, Hematemesis, Portal Hypertension, Cirrhosis

INTRODUCTION

Cirrhosis is common in this part of the world and so are its complications\(^1\)-\(^3\). About 40% of the patients of compensated cirrhosis and 60% of decompensated cirrhosis have varices\(^4\). Bleeding from varices carries a high mortality\(^5\). Despite advancements in management the mortality rate is still about 20% from the first variceal bleed\(^6\)-\(^7\). Highest risk of mortality is present during the first 5 days of an episode of bleed with gradual decline in risk over the period of 4-6 weeks\(^8\).

Many criteria and definitions to evaluate failure to control and prevent variceal bleed were developed in Baveno Consensus Workshops I-III\(^9\)-\(^12\). Those were later found out to be of limited clinical value in subsequent clinical trials and failed to gain popularity in clinical practice\(^13\). This led to the development of new criteria in Baveno-IV workshop in which an independent factor of Adjusted Blood Requirement Index (ABRI) was added. ABRI value of \(= 0.75\) at any point time was defined as failure of variceal bleed control. ABRI has been suggested as an independent criterion to determine failure to control variceal bleeding\(^14\).
ABRI has not been tested in our settings. We conducted this study to evaluate the ABRI and to correlate it with the treatment interventions and outcomes in acute variceal bleeding.

**PATIENTS AND METHODS:**

This cross-sectional study was conducted in Medical Unit IV, Civil Hospital Karachi associated with Dow University of Health Sciences, from January 2004 to October 2006. Records of all the patients admitted with acute variceal bleeding were retrieved. Patients with hepatocellular carcinoma, associated peptic ulcer and upper gastrointestinal (GI) malignancies were excluded.

Data were extracted on a specially designed proforma which included fields for hemoglobin and hematocrit on admission and on discharge/expiry, number of blood units transfused during admission, use of vasoactive agents (terlipressin/octreotide), endoscopic band ligation (EBL) and outcome (discharged/expired) were recorded. Child’s Class of the patients were determined. ABRI was calculated by the following formula:

\[
\text{ABRI} = \frac{\text{Blood Units Transfused}}{\left[\text{Final Hematocrit} - \text{Initial Hematocrit}\right] + 0.01}
\]

Continuous variables were compared for the difference of means by Student’s ‘t’ test. Means ± standard deviation (SD) were calculated for hemoglobin and hematocrit on admission and discharge/expiry. Mean ABRI were compared by ‘t’ test according vasoactive therapy, EBL and outcome. Correlation of ABRI with the same variables was also studied by plotting Receiver Operating Curves (ROC). SPSS version 15.0 was used for statistical analysis.

**RESULTS**

Seventy six patients fulfilling the inclusion criteria were selected. The rest were excluded due to incomplete data (18), hepatocellular carcinoma (2) and associated peptic ulcer (1).

The mean ± SD of hemoglobin, hematocrit, blood pack transfused and ABRI are given in Table I. Details of Child’s Class with outcome is given in Table II. Octreotide was given in 63 (82.9%) patients while 13 (17.1%) patients received terlipressin. The mean ABRI value in patients who received octreotide was 0.25 ± 0.08 while that in patients who received terlipressin was 1.09 ± 1.03 ‘t’ test did not reveal any significant difference of ABRI values between the two group (95% CI -2.2 to 2.56; P = 0.63).

<table>
<thead>
<tr>
<th>Table 1: Mean ± Standard deviation of continuous variables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>Hemoglobin on Admission</td>
</tr>
<tr>
<td>Hematocrit on Admission</td>
</tr>
<tr>
<td>Hemoglobin on Discharge/Expiry</td>
</tr>
<tr>
<td>Hematocrit on Discharge/Expiry</td>
</tr>
<tr>
<td>No. of Transfusions</td>
</tr>
<tr>
<td>ABRI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Cross tabulation of Child’s Class with outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child Class</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Child Class A</td>
</tr>
<tr>
<td>Child Class B</td>
</tr>
<tr>
<td>Child Class C</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

EBL was done in 22 (28.9%) of patients. ABRI in patients in whom EBL was done was 0.37 ± 2.12 while in patients in whom EBL was not done it was 0.41 ± 6.47. No statistically significant difference was found between the two (95% CI -2.78 to 2.86; P = 0.98). Thirty nine patients (51.3%) were discharged from the hospital and 37 (48.7%) expired. ABRI values for those who were discharged from the hospital were 0.60 ± 7.42 while its value in those who expired was 1.45 ± 1.99. The difference did not reach the statistical significance (95% CI -4.56 to 0.47; P = 0.11).

The ROC graphs were plotted to study the correlation of ABRI with vasoactive drugs, EBL and outcome.

Significant correlation ABRI was determined only with mortality. Area under the curve was 0.64, 95% CI 0.52 to 0.77 and P = 0.031. ROC plot of ABRI with mortality is shown in Figure 1.

Figure 1: ROC Curve of ABRI with Mortality.
DISCUSSION

Many criteria were developed for assessment of bleeding control in various Baveno Consensus Workshops\cite{1,11}. The goals of the Baveno workshops were to develop consensus definitions of key events related to portal hypertension and variceal bleeding, and to produce guidelines to facilitate the conduct and reporting of clinical trials. The consensus definitions concern the diagnosis of active bleeding, failure to control bleeding, the criteria to distinguish continuing bleeding from re-bleeding\cite{15}. Earlier Baveno I to III workshops failed to achieve those objectives and were modified in Baveno IV Consensus Workshop\cite{13}. The criteria of failure to arrest variceal bleeding included fresh hematemesis = 2 hours after start of treatment, 30 g drop in hemoglobin (\(-9\)% drop in hematocrit) if no transfusion is administered, death and ABRI = 0.75 at any time point\cite{14}. Baveno IV criteria were recently modified for application to pediatric population with portal hypertention\cite{17}.

In this study we tried to independently assess the values of ABRI with various variables. The results showed higher values of ABRI in patients who received terlipressin as compared to octreotide but it was not statistically significant. Similarly significance was not found when ABRI values were compared for EBL and outcome. The only significance was found in its correlation with mortality on ROC curve with significantly larger area under the curve for mortality.

The only other evaluation of ABRI done has shown low congruence between ABRI and other Baveno criteria and the incidence of treatment failure was reported to be higher than the previously reported frequencies of early re-bleeding. The authors were of the opinion that the criterion related to the quantity of blood transfusions was not a reliable indicator of treatment failure\cite{18}.

This study showed correlation with number of blood transfusion. It correlated well by giving higher scores to patients who expired. Being a public sector hospital patients were received in usually more serious condition as 39 were in Child's Class C who were unfit to undergo EBL. This is also the reason that the mortality rate in this study was on the higher side.

The limitations of this study include a retrospective analysis with comparatively limited sample size. Although it provided baseline data about ABRI correlation with different variables, prospective studies with appropriate power and sample size should be conducted to validate this new easy to use tool.

CONCLUSIONS:

ABRI correlated significantly with mortality in this study. No significant difference of ABRI values was found between the different treatment modes.

DISCLAIMER:

The study did not receive any financial support nor do any of the authors have any conflict of interest financial or otherwise for disclosure.

REFERENCES:


ORIGINAL ARTICLE

OVARIAN RESERVE IN FERTILE WOMEN AS DETERMINED BY ULTRASONOGRAPHY

Ambreen Usmani, Ishrat S. Shokh

ABSTRACT

Objective: To determine ovarian reserve in naturally fertile adult women.

Study design: Cross-sectional, analytical study.

Methods: Healthy fertile females (n = 70) aged 20-39 years with proven natural fertility were recruited between March and December 2006. Of these, 40 met the inclusion criteria. Total ovarian volume was calculated using the transabdominal and transvaginal ultrasound approach and an antral follicle count was performed transvaginally. The height and weight of each individual was taken to calculate the BMI, and the correlation made between ovarian volume (determined transvaginally) and the BMI.

Results: The women were divided into 2 groups of 20 each viz. between 20-29 years, and between 30-39 years. Total ovarian volume determined by transabdominal scan was 13 ±3.46 ml and 7.92 ±2.0 ml respectively in the two groups, and by transvaginal route was 15.13 ±4.37 ml and 9.97 ±2.99 ml respectively (p-value of both was 0.001). The AFC was 9.40 ±2.37 and 5.3 ±2.05 in the two groups (p-value 0.001). The BMI of the 2 groups was 23.4 ±2.97 and 24.4 ±3.8 (p-value 0.421). The correlation between ovarian volume and BMI was -0.40 (p-value 0.05).

Conclusion: Ovarian volume and antral follicle count were reduced significantly in the older age group; there was no difference between the BMI of the two age groups. When BMI of all women was plotted against ovarian volume, a decrease in the ovarian volume was observed with an increase in BMI.

Key words: Ovarian volume, ovarian reserve, antral follicle count, ultrasound.

INTRODUCTION

Ovarian reserve is an estimate of the primordial follicle pool in the ovaries. It is a relatively new concept and is used as a reflection of a woman's reproductive age and her remaining reproductive lifespan. It can be determined by several methods: directly by an ovarian biopsy, by sonographic visualization and measurement of the ovaries and calculation of ovarian volume, antral follicle count, mean follicular volume, or indirectly by biochemical assessment of follicle stimulating hormone, estrogen, anti-mullerian hormone and inhibin-B.

The human ovary contains a fixed pool of primordial follicles, maximal at five months of intrauterine life, and numbering around 701,000 at the time of birth. This pool reduces to 250,000-300,000 at the time of menarche, and then declines in a bi-exponential fashion with increasing age. At 37-38 years of age, it contains about 25,000 follicles. At this number, the follicular depletion accelerates, and menopause has been estimated to be about 12-14 years away. At a mean age of 50-51 years, only a few hundred or a thousand follicles remain. This age may vary in different populations and countries, and according to a study conducted in Lahore, it was found to be 49 ± 3.6 years in Pakistani women. The follicles in various stages of growth constitute the bulk of ovarian volume. A decline in the number of observable follicles due to atresia (death by apoptosis) occurs concomitant with advancing age. Thus ovarian volume decreases with increasing age. This was demonstrated by Pavlice et al. in a population of 13,963 conducted on women between 25 and 91 years of age by annual transvaginal sonography. A statistically significant decrease in ovarian volume was shown with each decade of life from age 30 to 70 years. Mean ovarian volume was 6.6 ml in women <30 years old, 6.1 ml in women 30-
SUBJECTS AND METHODS

The women were recruited between March 2006 to December 2006 from the outpatient departments of Ziauddin Memorial Hospital, Nazimabad, and Rahat Hospital, Karachi, until the desired number was obtained. A few women were volunteers from Ziauddin University Hospital.

The inclusion criteria were age between 20-39 years, regular menstrual cycles varying from 21-35 days, proven natural fertility with at least one pregnancy carried to term, each pregnancy having arisen spontaneously within 1 year after the start of unprotected intercourse and hormonal contraception, if taken, stopped 2 months before entering study protocol.

Exclusion criteria were evidence of endocrinological disease, secondary sub-fertility, history of ovarian surgery, and a history of hypertension, diabetes mellitus and smoking. In addition, women with ovaries of abnormal morphology on ultrasound examination were excluded.

The subjects were scanned on a complimentary basis at the Ultrasound Clinic, of Karachi. A written informed consent was obtained from all the subjects. Sonography of the ovaries was carried out on a day between the 2nd to 7th day of the menstrual cycle. All sonographic measurements were performed using Toshiba EcoCee and PowerVision 6000. The probes were multi-frequency, the transabdominal probe with a mid frequency of 3.75 MHz and the transvaginal probe with a mid frequency of 7.5 MHz.

The examination was performed transabdominally on an adequately full urinary bladder and transvaginally after emptying the bladder. Each ovary was scanned in 2 planes in which the longest dimension of the ovary was visible was frozen, D1 (depth) and D2 (anteroposterior) measurements were taken. The probe was then rotated through 900 and D3 (height) was measured. The volume of each ovary was calculated from the three dimensions by applying the equation for the volume of an ellipsoid (viz: $V = \frac{1}{2} \pi D1 \times D2 \times D3 \times 0.523 \text{ cm}^3$). The total ovarian volume was the sum of volume of the two ovaries. On transvaginal scan the volume was assessed, and the antral follicles (measuring between 2-10 mm in diameter) in each ovary were counted. The sum of antral follicles in the two ovaries was taken as the antral follicle count.

This study was conducted on healthy fertile women between the ages of 20 - 39 years. Ultrasound was used to visualize the ovaries, calculate their total volume, and to perform an antral follicle count. Its objective was to establish normal values in healthy fertile women, and observe the difference, if any, in two subsets of women viz. between 20 - 29 years and 30 - 39 years.

The reduction in number of primordial follicles is accompanied by a reduction in fertility. For any given age, the size of the follicle pool can be estimated by a mathematical model of decline. Theoretically, this could help in estimating the reproductive capacity of a woman at a given age; this in turn could assist in predicting a woman's chances of conception during a spontaneous cycle, and a possible outcome in assisted conception. It would also be of value in counseling those considering postponement of child-bearing for any reason.

The follicle growth pattern in the menstrual cycles in women of the reproductive age has been demonstrated by the ultrasonographic technique. At each cycle, several follicles are recruited, and grow at a rate of 2 - 6 mm daily in women in mid reproductive life (22-34 years); ovulation occurs at a mean follicular diameter of 16-27 mm.

The antral follicular count i.e. the total number of follicles between 2 – 10 mm in diameter the two ovaries is a parameter which has been used as a reflection of reproductive age. Ruess reported a significant reduction in number with age in a group of women 22 - 42 years of age. These differences in follicle counts were independent of the stage of menstrual cycle. Scheffer performed a study on 162 women in the follicular phase and reported a mean yearly decline of antral follicle count of about 5%, which increased to almost 12% after the age of 37 years. Several studies have determined the relation between ovarian volume and BMI and has shown a strong negative relation between the two, thus there is a decrease in ovarian volume with an increase in BMI. This may have clinical significance, as obesity has been shown to affect the fertility of a woman.
The height and weight of all subjects was taken and the body mass index (BMI) calculated from the \(\text{kg/m}^2\) formula\(^{19}\).

The data feeding and analysis was done on computer package SPSS 11.0 for Windows. The results were given in the text as mean, standard deviation of quantitative variables (age, weight, height, BMI, ovarian volume, and antral follicle count). Mean and standard deviation of quantitative variables between groups (20-29 and 30-39 years) were compared by ANOVA test. The correlation coefficient of ovarian volume, antral follicle count vs. age and BMI was determined. In all statistical analysis, p-value < 0.05 was considered significant.

This study was approved by the ethical committee of Ziauddin University.

**RESULTS**

A total of 70 women were recruited. Of these, 30 subjects were excluded: 7 subjects did not come for the scan; in 3, one of the ovaries could not be visualized on ultrasound examination, and 20 had abnormal ovarian morphology (polycystic ovaries in 18 and ovarian enlargement due to the presence of cysts in 2).

Table I shows the results of ovarian volume (measured transabdominally and transvaginally), the antral follicular volume (measured transvaginally) and the calculated BMI in the two subsets of women. Significant difference was seen in the total ovarian volume and the AFC in the 2 subsets of women, the volume and count being lower in the older women. There was no difference in the BMI of the two subsets.

The results of correlation between BMI and ovarian volume showed a negative value (-0.399) as shown in Fig. 1.

**DISCUSSION**

We estimated ovarian reserve by calculating ovarian volume and carrying out an antral follicle count (AFC) by an ultrasound examination in healthy fertile women not using hormonal contraception.

We compared the results in two subsets of women: i) between ages 20-29 years, and ii) between ages 30-39 years, and showed a significant reduction in total ovarian volume and AFC in the second group. This negative correlation of ovarian volume\(^{11}\) and of AFC with age is in keeping with the concept of reproductive ageing, and has been shown in several studies conducted during the past few years\(^{10}\).

Scheffer et al\(^{1}\) compared the mean values and ranges of several sonographic parameters for 3 age groups: young (25 – 34 years), middle-aged (35- 40 years) and the old (41 – 46 years). The total ovarian volume in the third older group differed significantly from that in the two younger groups, measuring 11.8, 11.4 and 8.3 ml respectively. The number of antral follicles differed significantly in all three groups (the count being 15, 9 and 4 respectively). The total follicular volume showed a decrease with increasing age (0.71, 0.58 and 0.39 ml), the decrease in volume being less steep than the drop in follicular count. They concluded that the antral follicle count was valuable in assessing ovarian reserve, and its use as a single test to predict response to controlled ovarian stimulation and the probability of pregnancy in assisted reproduction seemed rational.
We rehashed the data to make the age groups comparable to those of Scheffer et al. Ovarian volume calculated for groups 25-34 years and 35-39 years was 10.49±2.72 and 7.47±3.8 ml respectively; these values were a little less than those of Scheffer et al’s, but the difference was not statistically significant.

A comparison of ultrasound with other tests for detecting ovarian reserve shows ultrasound to be of great value as it is non-invasive, easily performed and reproducible, readily available, and inexpensive\(^{20,21}\). Biochemical tests such as FSH, estrogen, anti-mullerian hormone and inhibin -B\(^{12}\) are relatively expensive and not all are freely available in the laboratories of our country. Ovarian biopsy as a test of ovarian reserve is no longer practised, as it is invasive, carries the risk of adhesions, and the distribution of follicles in the ovarian tissue could be irregular and not representative of the total reserve\(^{21-24}\).

The limitations of this study include the exclusion of age group above 40 years, and the failure to record the waist hip ratio (WHR); thus the relation between ovarian reserve and WHR could not be estimated. Although BMI and ovarian volume showed a negative value of 0.40, it is possible that WHR and ovarian reserve may have demonstrated a better correlation.

**CONCLUSION**

The ovarian reserve in the menstrual phase determined by sonographic measurements of ovarian volume and antral follicle count was significantly decreased with age. The ovarian volume also showed a decrease with an increase in the BMI, indicating the possible decrease in fertility with an increase in the woman’s weight.

**ACKNOWLEDGMENT**

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**REFERENCES**


13. Lenz S. Ultrasonic study of follicular maturation, ovulation and development of corpus luteum during.


RIGHT VERTEBRAL ARTERY: ANOMALOUS PREVERTEBRAL COURSE AND DISTRIBUTION

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ABSTRACT
Vertebral artery (VA) is the largest branch of the first part of the subclavian artery and the chief source of blood supply to brainstem, cerebellum, occipital lobe of cerebrum and posterior cranial fossa. Anomalous origin, course and/or branching pattern of VA may lead to disturbance in vertebro-basilar hemodynamics, risking cerebro-vascular insufficiency. A unique case of right VA having usual origin, but anomalous course and branching pattern in its prevertebral segment is described. Moreover the right thyrocervical trunk was absent in present case and inferior thyroid artery branched off the variant VA. The ligation of such vertebral artery may cause a compromise to thyroid in addition to posterior cranial fossa blood supply. The information about its course is crucial during diagnostic investigations and surgical procedures in the head and neck region.

Key words: vertebral artery, inferior thyroid artery, anomalous course

INTRODUCTION
Vertebral artery (VA), the 1st and largest branch of subclavian artery, arises from its posterosuperior aspect and runs upward and medially to enter the foramen transversarium of 6th cervical vertebra1. It ascends through the succeeding foramina transversaria of upper cervical vertebrae. Leaving the foramen transversarium of atlas, it ascends, cranially through foramen magnum to reach the brainstem to join its fellow to form the basal artery at ponto-medullary junction. The first segment of vertebral artery from its origin from subclavian artery (SA) to entry into respective foramen transversarium is called prevertebral segment, which is frequently affected by atherosclerosis2. The prevertebral segment of VA is followed by the vertebral and intracranial segments. VA may enter any of the foramen transversarium of 6th cervical (87.5%), 5th cervical (6.6%), 4th cervical (0.5%) and 7th cervical (5.4%)3.

Prevalence of anomalous vertebral arteries has been investigated by many researchers4. Although ectopic origin of VA is uncommon, two variants have been frequently reported origin of left vertebral artery from the arch of aorta and right vertebral artery from right common carotid artery4. Although the incidence of anomalous origin of VA is relatively more than its anomalous tortuous course, failure to recognize a medically located vertebral artery may result in life threatening iatrogenic injury during spinal decompression5. Laceration of VA is the most challenging surgical dilemma during anterior cervical spinal surgery. Massive hemorrhage from ruptured VA might lead to uncertain neurological morbidity7. Therefore preoperative recognition and appropriate modification of anterior decompression of spine can yield excellent clinical results without risking significant complications. During imaging studies, surgery or cadaveric dissection in anatomy laboratory, the detection of anomalous VA is usually an incidental finding. Although most cases are clinically asymptomatic, they can initiate thrombo-embolic phenomenon, risking cerebral ischemia8.

The present case report represents a unique case of right VA with anomalous course and branching pattern in its prevertebral segment, detected by cadaveric dissection.

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CASE REPORT

Forty eight bodies of different ethnic origin were dissected in the laboratories of Human Anatomy, Shifa College of Medicine, Islamabad, Sir Syed College of Medical Sciences for Girls, Karachi, and College of Medicine, King Saud University, Riyadh, KSA from January, 2005 through August, 2007. There was a single case of unilateral anomalous right vertebral artery in a 55-year Caucasian male. The anomalous right vertebral artery had usual origin from superior aspect of the first part of right subclavian, with an external diameter of 8 mm at its origin, ascending vertically upward (with slight lateral inclination) between longus colli and scalenus anterior muscles to the level of superior border of thyroid cartilage (the level of bifurcation of right common carotid artery) where it turned posteriorly and entered into the foramen transversarium of 4th cervical vertebra. The prevertebral segment of anomalous right vertebral artery (ARVA) was not tortuous; however it gave origin to right inferior thyroid artery (about 2.5 cm distal to its origin from subclavian artery) which proceeded medially to reach the inferior pole of right lobe of thyroid gland. This anomalous right inferior thyroid artery was also very tortuous and was cramped between two terminal divisions / branches of right recurrent laryngeal nerve, close to inferior pole of thyroid gland (Fig 1). The thyrocervical trunk was missing in right subclavian artery (Fig 1-3).

The rest of the human body had a normal anatomy.

DISCUSSION

To understand the anomalous development of VA, knowledge of embryological transformation of aortic arches into adult arterial system is essential. Embryologically, right subclavian artery develops from right 4th aortic arch, proximal right dorsal aorta and right 7th intersegmental artery (Fig. 2). Usually the 1st part of right VA develops from proximal part of dorsal branch of 7th cervical intersegmental artery proximal to postcostal anastomosis. The vertebral part of vertebral arteries develops from postcostal longitudinal anastomosis between 15th to 7th cervical intersegmental arteries and the cervical intercostals obliteration zone10. During this process, the caudal part of the dorsal aorta is obliterated just before its confluence with the left dorsal aorta, and the 7th intersegmental artery continues as right subclavian artery10. Lenke et al schematically depicted different variants of ARVA cited in published scientific literature5 (Fig 3).

In most cases published in the medical literature, anomalous vertebral artery did not result in clinical symptoms11. Rarely, patients complain of dizziness, having no correlation to the anomalous origin of the vertebral artery. Anomalous origin and distribution of VA

Figure 1:
The anomalous right vertebral artery giving origin to inferior thyroid artery.
can exhibit cerebral insufficiency due to changes in vertebro-basilar hemodynamics, however, there is no conclusive evidence that these variants lead to a predisposition to cerebrovascular accidents. Anomalous VA may be an independent risk factor for arterial dissection. The true value of detecting anomalous variants is the diagnostic gain prior to the surgery of supra-aortic arteries. In present case right thyrocervical trunk was absent and inferior thyroid artery branched off the right VA, which is a unique finding. For anomalous inferior thyroid artery originating from the vertebro artery, ligation of the vertebro artery may cause compromised supply to thyroid in addition to compromised blood supply to posterior cranial fossa. Existing literature and the present study reflects the scarcity of anomalous VA in Asians (0.02%) as compared to Caucasians (2.4 – 5.8%). Detailed knowledge of an anomalous origin and distribution of supra-aortic arteries is of importance for patients who have to undergo digital subtraction angiography (as an emergency procedure) to rule out the possibility of intracranial aneurysm after subarachnoid hemorrhage.

In summary, although anomalous vertebral artery is an anatomic variant, detailed information is crucial during diagnostic investigations and surgical procedures (especially vascular surgery) in the head and neck region.

ACKNOWLEDGEMENT

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REFERENCES


3. Agur AMR. Grant's atlas of anatomy. 9th Ed. Baltimore: Williams & Wilkins, 1991; 560


PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS

Iqbal A. Memon, Samina Tariq

ABSTRACT
A case of progressive familial intrahepatic cholestasis (PFIC) is described in a 7 years old girl who presented with pruritis and progressive jaundice alongwith failure to thrive. Laboratory indicated PFIC type 1 or 2 along with cirrhosis. Patient is responding to supportive therapy while liver transplantation is being awaited.

Key words: Progressive familial intrahepatic cholestasis, failure to thrive, jaundice, cirrhosis.

INTRODUCTION
Cholestasis is either an alternative or concomitant response to injury caused by extrahepatic or intrahepatic obstruction to bile flow. Progressive familial intrahepatic cholestasis (PFIC) is an important cause of cholestasis and biliary cirrhosis in pediatirc age group. A high index of suspicion is required in the diagnosis of PFIC as neonatal cases as well as older children are usually misdiagnosed and thus malnourished for a long time thus narrating a long history of suffering.

A case of Progressive Familial Intrahepatic Cholestasis is described in which the patient presented with pruritis and progressive jaundice alongwith failure to thrive. PFIC 3 was ruled out due to normal gamma GT. PFIC 1 or 2 could not be differentiated as histopathology was confounded due to fibrosis setting in.

CASE REPORT
A 7 year old girl presented with itching all over the body for 7 months, anorexia for 3 months and progressive jaundice with dark yellow urine for the last 1 month. There had been repeated self limited episodes of jaundice each lasting a few weeks since later infancy. An undocumented liver biopsy was done at 1 year of age. She had 2 healthy siblings out of a consanguineous parentage. There was no family history of jaundice.

Physical examination revealed a thin underweight girl who was deeply jaundiced with scratch marks all over her body. She was active alert, and well oriented. She had normal vital signs with weight of 17 kg. (< 5th percentile) and height of 110 cm ( < 5th percentile) indicating failure to thrive. Liver was 1 cm palpable with a span of 11 cm. Rest of the physical examination was unremarkable.

The working diagnosis was cholestatic jaundice. The hemoglobin was 10.4 gm%, MCV 82.8 fl, MCH 28.9 pg, MCHC 34.9 gm/dl, TLC 9.2x10^3 /mm³, platelets 374.00 x 10^3 /mm³, urea 28 mg%, creatinine 0.4 mg%, potassium 3 meq%, sodium 136 meq%, bicarbonates 19 meq%, serum calcium 9.5 mg%, bilirubin total 12 mg% with direct bilirubin of 10 mg%, alanine aminotransferase (ALT) of 33 u/l, aspartate amino transferase 75 u/l, alkaline phosphatase 1183 u/l, gamma glutamyltransferase (gGT) of 31 U/L with prothrombin time (PT) of 16/13 sec and serum cholesterol of 116 mg/dl. Liver biopsy revealed moderate periportal inflammation with extensive septal fibrosis focally and nodule formation. There was marked bile stasis, and bile ducts were reduced with no evidence of malignancy, i.e. moderate active inflammation with impending fibrosis stage III and IV and marked bile stasis.

She showed partial improvement on supportive therapy like cholestyramine, phenobarbitone, nutritional advice and vitamin/mineral supplements. She is a candidate for liver transplantation as cirrhosis has already started taking its roots in the liver.

DISCUSSION
Cholestasis may be due to infectious, genetic, metabolic or undefined abnormalities giving rise to either mechanical obstruction of bile flow or to functional impairment of hepatic biliary function and bile secretion. PFIC is an
important cause of cholestasis and biliary cirrhosis in pediatric group\(^2\). Cholestasis is caused by impaired bile secretion associated with, and often secondary to, intracellular accumulation of bile acids in hepatocytes\(^2\). It represents a group of diseases affecting membrane transport proteins involved in bile formation and falls into the category of non-syndromic paucity of interlobular bile ducts. It presents as hepatocellular cholestasis; often in the neonatal period causing liver failure at variable age, ranging from infancy to adolescence and eventually may result in death\(^4\).

This entity is often overlooked and labeled as biliary atresia or neonatal hepatitis. Misdiagnosis is the result of sub-optimal ultrasonography and non-visualization of gallbladder on Hepatic iminodiacetic acid (HIDA) scan due to poor uptake by hepatocytes\(^5\).

Adolescents with conjugated hyperbilirubinemia should be evaluated for acute and chronic hepatitis, alpha-1-antitrypsin deficiency, Wilson disease, liver disease associated with IBD, autoimmune (AIH), syndromes of intrahepatic cholestasis, cholelithiasis, abdominal tumours, enlarged lymph nodes or hepatic inflammation from drug ingestion\(^5\).

PFIC is an autosomal recessive condition and is classified as 3 types i.e. types 1, 2 and 3. The differentiation is on clinical grounds and laboratory findings. PFIC-1 is due to a defect of familial intrahepatic cholestasis-1 gene, (FIC-1{ATP8B1}) which is localized on chromosome 18\(^8\). FIC-1 activates the transcription of the FXR (Farnesoid X receptor), an important modifier of bile acid homeostasis gene\(^6\). In PFIC-2 the gene defect lies at chromosome 2 q24, the FIC-2 locus\(^8\). Gene ABCB 11 defect is in the canalicular ATP-dependent bile acid transporter BSEP (bile salt export promoter)\(^7\). PFIC-3 is characterized by elevated serum gGT. Early, PFIC-3 is associated with MDR-3 gene (ABCB4) deficiency\(^7\).

This genetic mapping could not be conducted in the present case. The girl had presented in childhood with failure to thrive, progressive jaundice and cirrhosis. Due to the undocumentation of liver biopsy in the infancy, it could not be ascertained with surety as to whether it was type 1 or 2 PFIC. The present histopathology had such marked changes of cirrhosis that the distinction could not be made. This case emphasizes the importance of early diagnosis and documentation to retard irreversible changes in a potentially fatal condition.

REFERENCES


CASE REPORT

BONE SCAN: A SENSITIVE MODALITY FOR DIAGNOSING AND PREDICTING OUTCOME FOR REFLEX SYMPATHETIC DYSTROPHY

Maseeh uz Zaman, Riffat Hussain, M. Nadeem Ahmad, Khalil Khan, Gufran Khan

ABSTRACT
Reflex sympathetic dystrophy is a consequence of overactive sympathetic nervous system that results in burning pain, stiffness, swelling and discoloration of the affected limb. This case report describes the condition in a man that was diagnosed with the help of radionuclide bone scan.
Key words: reflex sympathetic dystrophy, complex regional pain syndrome, radionuclide bone scan.

INTRODUCTION
Reflex sympathetic dystrophy (RSD) or complex regional pain syndrome is a condition of burning pain, stiffness, swelling and discoloration of the affected limb (commonly hands and feet). Females are affected more commonly than males (3:1). Only one in five affected patients is able to return to a normal level of functioning. It occurs from a disturbance in the sympathetic (overactive) nervous system that controls the blood flow and sweat glands. It often follows a trauma or surgery. Other causes include pressure on a nerve, infection, post-burn injury, neck disorder, stroke and myocardial infarction. Diagnosis is made on physical examination, X-rays, bone scans, CT scan, MRI and sympathetic blockade. Bone scan is highly sensitive (96%) and specific (98%). It is also a useful guide to prognosis. About 90% of patients with positive bone scan experience a favorable response to steroid as oppose to 34% of those with negative scintigrams.

CASE REPORT

This 42 years old male presented with 6 weeks history of severe burning sensation and pain in the left hand. He had a laminectomy over C5-C7 about 10 weeks back. Follow up MRI revealed no nerve compression. X-rays of the left hand was unremarkable (Fig. 1). A three phase bone scan was performed with 720 MBq of Tc-99m MDP using a large field of view digital gamma camera. Dynamic
Reflex Sympathetic Dystrophy

and blood pool images revealed abnormally increased blood flow over left forearm, wrist and hand (Fig. 2a and 2b). Delayed images revealed diffusely increased tracer uptake over the left wrist, carpal, metacarpophalangeal and inter-phalangeal joints (Fig.2c). A diagnosis of reflex sympathetic dystrophy was made. He was started on an oral steroid therapy with analgesic for 3 months and responded well to the treatment.

DISCUSSION

Reflex sympathetic dystrophy has been considered as a distinct entity since the description by Mitchell. It has three clinical stages and bone scan findings will vary depending upon the phase.

Stage 1 (acute) may last up to 3 months. In this stage there will be pain, swelling, burning, excessive sweating and restricted movement of the area. Bone scan shows increased blood flow, blood pool and enhanced tracer uptake in the delayed images in the peri-articular region. Decreased flow and blood pool activity may be seen uncommonly (1-8%) particularly in young patients and hemiplegics.

Stage 2 (dystrophic) can last from 3-12 months. Swelling is more constant, skin wrinkles disappear, skin temperature becomes cooler and nails become brittle. The pain becomes more widespread. Bone scan shows normalization of flow and blood pool activity but increased activity on delayed images persists.

Stage 3 (atrophic) occurs from 1 year onwards. The skin of the affected area becomes pale, dry, tightly stretched and shiny. The area is stiff, pain may decrease and there is less hope of getting motion back. Flow and blood pool activity can be normal or decreased (in about 33% cases) and delayed images show normal or decreased tracer uptake. Persistent increased activity on delayed images has been reported in up to 40% patients. This reduced flow in advanced RSD is may be related to amyotrophy caused by disuse.

In the evaluation of children for RSD, increased activity in all 3 phases of bone scan is seen in only 20% cases. A pattern of decreased flow, blood pool and delayed activity is more characteristically seen in children.

Therefore, we conclude that the three phase bone scan is a safe, non-invasive, cost effective, highly sensitive and specific modality for the diagnosis of reflex sympathetic dystrophy and also a good predictor of response to treatment as shown in this case.

REFERENCES


BLOOD DONOR SCREENING FOR HEPATITIS AND HIV

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Donated blood, all over the world, is routinely screened for several infections depending on the endemicity and/or prevalence; these tests vary from continent to continent. The first and the most important commandment in blood donor selection is that, the donor should be in a state of good health both medically and surgically. Donors that have any disease such as viral hepatitis, malaria, venereal disease, AIDS are excluded from blood donation. Pregnancy, lactation, infection, and blood donation within less than 12 weeks are temporary contra-indications for blood donation.

Hepatitis B and C are major health problems globally. In Pakistan, there are 4.5 million estimated carriers with a carrier rate of 3-4%. Blood and its products are the most important vehicle for transmission of HBV, HCV and HIV. Routine screening of blood donors has led to identification of persons with anti-HCV and asymptomatic, therefore, the present study was designed to evaluate blood screening practice and outcome from donated blood at a private laboratory.

It was a cross sectional study including 688 blood donors reporting in Fatima laboratory located at Baqai Medical University Karachi, during the period of January to December 2006. Five ml. of venous blood was drawn by aseptic technique. The tests performed for screening purpose included: ABO grouping and Rhessus typing, Hepatitis B surface antigen (HBsAg) antibody to hepatitis C virus (Anti-HCV) and antibody to human immunodeficiency virus (Anti-HIV). The qualitative analysis for HBsAg, HCV and HIV were performed on test device (ACON Company) by immunochromatographic technique.

All the donors were deferred and accepted for blood transfusion according to the screening results. Thirty one (4.50%) were positive for HBsAg, 30 (4.36%) were positive for anti HCV and 1 (0.14%) were positive for anti HIV (Table-1).

According to the above observations, frequency of HBsAg (4.5%) was greater when compared with HCV and HIV. There are 400 million HBV carriers worldwide, of which more than 250 million reside in Asia. In Northern Pakistan the prevalence of HBsAg was 2.5%. Therefore, donors must be screened before blood transfusion even if they are healthy looking. In our study, 30 blood donors were found to be anti HCV - reactive. Screened blood bags received from other transfusion centers showed higher rates 4.27% of hepatitis viral infection.

In the present study, frequency of hepatitis C viral infection among blood donors found to be reactive 4.36% and HIV (0.14%). The rate of HCV during screening also observed in another study was 4.2% which is in confirmation of our results. Pakistan despite being a densely populated country, has a low to moderate sero-prevalence of HIV/AIDS. By June 2005, only 2086 cases of HIV and AIDs were reported throughout the country. The risk of HIV transmission through blood transfusion has been estimated to be 1 in 1.3 million blood donors. In conclusion screening of blood donors and deferral procedures is meant to minimize the risk of transmitting an infectious agent from donated blood to the recipient, as well as ensuring the welfare of the donor. People donating blood may seem healthy but they might be the carriers of HBsAg, HCV or HIV.

It is recommended that all the blood transfusion services must follow internationally acceptable standard procedures for screening of blood. Less specific and less sensitive methods for screening will misguide everyone and will promote transmission of these diseases in our population. Screening results of borderline cases must be rejected for blood donation. Different awareness programs should be created for the public about different risk factors of these diseases.
REFERENCES:


LETTER TO THE EDITOR

PLAGIARISM

Sultana Habibullah

Sir,

Dow University of Health Sciences as a public sector medical University, has the credit of organizing multiple workshops on research methodology for postgraduates/faculty besides including it in the curriculum, in a short span of time. The main objective of all these exercises is to train their graduates to do original research work rather than to depend on the work of foreign researchers. Research is not a solo flight. It is an activity that involves many people and needs resources far beyond one’s personal possessions. Its documentation needs careful references to state a fact, giving credit to the writer from whom words or ideas have been borrowed. Unfortunately, instead of doing original work, other’s work is presented with a few changes and claimed authorship for many reasons. This misconduct in research is known as PLAGIARISM. It is Latin word meaning kidnapping. It is actually using someone else’s work as an author and it includes stealing of the ideas, thoughts, pictures, graphs and data without giving credit or acknowledgement to the creator. At undergraduate level, plagiarism can also be accidental but the commonest reason is laziness. People are not motivated to produce their own ideas, they just want to copy-cut-paste and complete their work to get credit. The best way to use references is to paraphrase the finding in own words, sequence and wording, give quotation marks if sentence is taken as it is and cite the source. If the source is not clear, this should be explicitly stated. If any specific help has been received from someone, he or she should be given due acknowledgement. There is one exception to this rule i.e. common knowledge. If the fact or idea is common knowledge, citation is not required. Common knowledge is a fact idea that appears in a general source like an encyclopedia or dictionary, is repeated by over three sources or claimed to be common knowledge by more than three authors.

Plagiarism devalues others’ original work. Submitting another writer’s work as ours is taking an unfair advantage over others who do their own work. Copyright violation can result in fines or damages. Even ignorance is no excuse. Intentional plagiarism is, when the source is known but not given citation; and it is un-intentional when the source is not known, like copying from web. Both are punishable. A charge of plagiarism can have serious consequences like expulsion from the institution; loss of job etc.

In future, great research contributions are expected to come from the students in JDUHS. To address the growing problem of plagiarism, it is the duty of teachers/supervisors to take steps to ensure, that the students have a clear understanding of plagiarism and they should be trained for drafting and note-taking skills.

REFERENCES

4. Plagiarism: its importance www.engl.niu.edu/comskills/students/plagiarism/Plagiarism.html.
The papers published in your journal are very informative.

Professor Dr. Saeeda Asadullah Khan
Vice Chancellor
Fatima Jinnah Women University
Rawalpindi

I found it quite informative and interesting, I compliment you for publishing a document of such a standard.

Engineer Muhammad Zakir Ali Khan
Vice Chancellor
Sir Syed University of Engineering and Technology Karachi

Its pages are replete with stunning information about the complicated diseases baffling our countrymen.

Professor Dr. Ihsan Ali
Vice Chancellor
Hazarat University Mansehra, NWFP

Your entire editorial board deserves credit for bringing out a research Journal of such high professional standards, which competes favorably with the standards of international Journals. We are also impressed by your panel of national and international Advisory Board, all whom are held in high esteem.

Ms Seema Maghul
Vice Chancellor
Greenwich University
Karachi

The first issue of JDUHS is no doubt a great contribution in each and every discipline of medical field.

Professor Dr. Asad Aslam Khan
(Sitar-e-Imtiaz)
Principal / Director General
College of Ophthalmology & Allied Vision Sciences (COAVS)
K.E.M.U / Mayo Hospital , Lahore

I hereby congratulate you for bringing such a nice medical Journal and hoping that the said Journal will be most beneficial to promote research work in the health care profession.

Professor Sikandar Ali Shaikh
Principal
Chandka Medical College Larkana

I am keeping this Journal in the Library for everyone to read.

Professor Humayun Maqbool
Principal
FMH College of Dentistry
Shadman, Lahore.

The editorial board and contributors deserve special appreciation for an impressive presentation both in terms of contents and quality. I am sure it will soon be recognized by PMDC and listed in Index Medicus.

Professor Musarrat Hussain Dean
Jinnah Postgraduate Medical Centre Karachi

I would like to congratulate you and your entire team for producing this timely Journal from the University. It is a very positive start indeed you and your entire team deserve congratulations.

Professor Dr. Syed M. Wasiq Jafri
Iba-e-Sina Professor
Chief of Gastroenterology
Chairman of Medicine
The Aga Khan University Karachi

I appreciate the quality of content and their presentation.

Brig. Azhar Mubarak
Editor, PAFMJ
Pakistan Armed Forces Medical Journal
Army Medical College Rawalpindi

I found the articles of good academic standard and was particularly impressed by the one tackling the ethical issues in medical health care.

Professor Abdul Sattar Memon
Professor of Surgery
Director Research & Editor
JLUMHS
Liaquat University of Medical & Health Sciences
Jammshoro

I must appreciate and admire the standard and presentation of the first issue of the Journal which is comparable to any other standard international Journal.

Professor Khalid Mahmood
Medical Unit V
Daw University of Health Sciences & Civil Hospital Karachi

This first issue of JDUHS is an excellent research oriented publication, which is a welcome addition to the scientific publication club of our country, the selection of the articles is excellent and overall it is an excellent publication.

Professor Dr. Ijaz Haider Rizvi
Dept. Forensics Medicine & Toxicology
Quaid-I-Azam Medical College Bahawalpur

It is very good addition in the list of medical Journals.

Dr. Muhammad Naeem Iqbal
Head of Pharmacology
Department
Punjab Medical College Faisalabad
16th Asian Pacific Congress of Cardiology  
December 13–16, 2007  
Taipei Taiwan  
Website: http://www.apcc2007.org

Medical Research Society of Pakistan  
18th Annual Meeting,  
December 29, 2007  
Center of Biomedical Ethics & Culture (CBEC, Sind Institute of Urology and Transplant (SIUT), Karachi  
Website: http://www.MRSP.org.pk

3rd International Family Medicine Conference  
January 25-27, 2008  
Website: www.aku.edu, E-mail: conf.sect@aku.edu

20th Annual National Conference 2007  
Pakistan Society of Neurosurgeons  
December 1-2, 2007  
Aga Khan University, Karachi  
E-Mail: neurocon2007@hotmail.com

Society of Surgeons of Bangladesh  
10th International Surgical Congress  
December 7-10, 2007  
Dhaka, Bangladesh  
Email: sosb@dhaka.net, ferozzequader@yahoo.com

Pakistan Orthopaedics – 2008  
22nd INTERNATIONAL ORTHOPAEDIC CONFERENCE & ASAMI (Int.)  
February 6-9, 2008  
Karachi  
www.pakorthocon2008.com

27th Annual Meeting  
Arthroscopy Association of North America  
April 24-27, 2008  
Washington, DC, USA

IPRAS 2009, The 15th World Congress of the International Confederation for Plastic, Reconstructive and Aesthetic Surgery  
November 29 - December 3, 2009  
New Delhi, India.: More Details:

Website: www.ipras2009.org ,  
E-mail : desk@ipras2009.org

International Symposium on  
Tropical Medicine and Hygiene  
December 12–15, 2007  
Aga Khan University, Stadium Road  
Karachi, Pakistan.  
E-mail: conf.sect@aku.edu

Anxiety and Comorbid Disorders:  
Understanding Risk, Optimizing Outcomes  
28th Annual Conference  
March 6-9, 2008  
Silver Spring, MD, USA. 240-485-1032,  
E-mail:mmartinez@adaa.org

5th Asia Pacific Medical Education Conference  
(APMEC)  
National University of Singapore  
Singapore  
E-mail:medbox10@yahoo.com

4th International CME & 8th National Meeting on  
Dermatopathology  
November 30-December 2, 2007  
New Delhi, India.  
E-mail:sujaykandpur@yahoo.co.in

Advances in Paediatric Surgery 2007  
December 1-3, 2007  
Chennai, India  
Email:kkeithsurgeon@yahoo.com

Eighth Shaukat Khanum Memorial Cancer Symposium  
November 14-16, 2007  
Peshawar, Pakistan  
Website:www.shaukathanum.org.pk

50th Golden Anniversary Congress (ICA 2008)  
International College of Angiology  
July 19–23, 2008  
Tokyo, Japan  
Email:denisecmrossignol@cs.com  
http://www.intcollegeofangiology.org
Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication

Updated February 2006

Publication Ethics, Sponsorship, Authorship, and Accountability

The following information is available to be viewed/printed in Adobe Acrobat PDF format.

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IX. Inquiries

I. A. About the Uniform Requirements

A small group of editors of general medical journals met informally in Vancouver, British Columbia, in 1978 to establish guidelines for the format of manuscripts submitted to their journals. The group became known as the Vancouver Group. Its requirements for manuscripts, including formats for bibliographic references developed by the National Library of Medicine, were first published in 1979. The Vancouver Group expanded and evolved into the International Committee of Medical Journal Editors (ICMJE), which meets annually. The ICMJE gradually broadened its concerns to include ethical principles related to publication in biomedical journals. The ICMJE has produced multiple editions of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Over the years, issues have arisen that go beyond manuscript preparation, resulting
Uniform Requirements

in the development of a number of Separate Statements on editorial policy. The entire Uniform Requirements document was revised in 1997, sections were updated in May 1999 and May 2000. In May 2001, the ICMJE revised the sections related to potential conflict of interest. In 2003, the committee revised and reorganized the entire document and incorporated the Separate Statements into the text. The committee prepared this revision in 2005. The total content of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals may be reproduced for educational, not-for-profit purposes without regard for copyright; the committee encourages distribution of the material. Journals that agree to use the Uniform Requirements are encouraged to state in their instructions to authors that their requirements are in accordance with the Uniform Requirements and to cite this version. Journals that wish to be listed on www.icmje.org as a publication that follows the Uniform Requirements should contact the ICMJE secretariat. The ICMJE is a small working group of general medical journals not an open membership organization. Occasionally, the ICMJE will invite a new member or guest when the committee feels that the new journal or organization will provide a needed perspective that is not already available within the existing committee. Open membership organizations for editors and others in biomedical publication include the World Association of Medical Editors www.wame.org and the Council of Science Editors www.councilofscienceeditors.org.

I.B. Potential Users of the Uniform Requirements

The ICMJE created the Uniform Requirements primarily to help authors and editors in their mutual task of creating and distributing accurate, clear, easily accessible reports of biomedical studies. The initial sections address the ethical principles related to the process of evaluating, improving, and practicing manuscripts in biomedical journals and the relationships between editors and authors, peer reviewers, and the media. The latter sections address the more technical aspects of preparing and submitting manuscripts. The ICMJE believes the entire document is relevant to the concerns of both authors and editors. The Uniform Requirements can provide many other stakeholders—peer reviewers, publishers, the media, patients and their families, and general readers—with useful insights into the biomedical authoring and editing process.

I.C. How to Use the Uniform Requirements

The Uniform Requirements state the ethical principles in the conduct and reporting of research and provide recommendations relating to specific elements of editing and writing. These recommendations are based largely on the shared experience of a moderate number of editors and authors, collected over many years, rather than on the results of methodical, planned investigation that aspires to be “evidence-based.” Wherever possible, recommendations are accompanied by a rationale that justifies them, as such, the document serves an educational purpose. Authors will find it helpful to follow the recommendations in this document whenever possible because, as described in the explanations, doing so improves the quality and clarity of reporting in manuscripts submitted to any journal, as well as the ease of editing. At the same time, every journal has editorial requirements uniquely suited to its purposes. Authors therefore need to become familiar with the specific instructions to authors published by the journal they have chosen for their manuscript—for example, the topics suitable for that journal, and the types of papers that may be submitted (for example, original articles, reviews, or case reports)—and should follow those instructions. The Mulford Library at the Medical College of Ohio maintains a useful compendium of instructions to authors.

II. Ethical Considerations in the Conduct and Reporting of Research

II.A Authorship and Contributorship

II.A.1. Byline Authors

An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study, and biomedical authorship continues to have important academic, social, and financial implications. In the past, authors were rarely provided with information about contributions to studies from those listed as authors and in acknowledgments. Some journals now request and publish information about the contributions of each person named as having participated in a submitted study, at least for original research. Editors are strongly encouraged to develop and implement a contributorship policy, as well as a policy on identifying who is responsible for the integrity of the work as a whole. While contributorship and guarantorship policies obviously remove much of the ambiguity surrounding contributions, it leaves unresolved the question of the quantity and quality of contribution that qualify for authorship. The International Committee of Medical Journal Editors has recommended the following criteria for authorship; these criteria are still appropriate for those journals that distinguish authors from other contributors.

- Authorship credit should be based on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content, and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript (3). These individuals should fully meet the criteria for authorship defined above and editors will ask these individuals to complete journal-specific author and conflict of interest disclosure forms. When submitting a group author manuscript, the corresponding author should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name. Journals will generally list other members of the group in the acknowledgments. The National Library of Medicine indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript.

- Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.

- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Some journals now also request that one or more authors, referred to as “guarantor,” be identified as the persons who take responsibility for the integrity of the work as a whole, from inception to published article, and publish that information.

Increasingly, authorship of multi-center trials is attributed to a group. All members of the group who are named as authors should fully meet the above criteria for authorship. The order of authorship on the byline should be a joint decision of the
Uniform Requirements

crash authors. Authors should be prepared to explain the order in which
authors are listed.

II.A.2. Contributors Listed in Acknowledgments

All contributors who do not meet the criteria for authorship should be
listed in an acknowledgments section. Examples of those who might
be acknowledged include a person who provided purely technical
help, writing assistance, or a department chair who provided only
general support. Editors should ask authors to disclose whether they
had writing assistance and to identify the entity that paid for this
assistance. Financial and material support should also be acknowledged.
Groups of persons who have contributed materially to the paper but
whose contributions do not justify authorship may be listed under the
heading such as “clinical investigators” or “participating investigators,”
and their function or contribution should be described—for example,
“served as scientific advisors,” “critically reviewed the study proposal,”
“collected data,” or “provided and cared for study patients.”
Because readers may infer their endorsement of the data and conclusions,
all persons must give written permission to be acknowledged.

II.B. Editorship

II.B.1. The Role of the Editor

The editor of a journal is the person responsible for its entire content.
Owners and editors of medical journals have a common endeavor—
the publication of a reliable and readable journal, produced with due
respect for the stated aims of the journal and for costs. The functions
of owners and editors, however, are different. Owners have the right
to appoint and dismiss editors and to make important business decisions
in which editors should be involved to the fullest extent possible.
Editors must have full authority for determining the editorial content
of the journal. This concept of editorial freedom should be resolutely
defended by editors even to the extent of placing their positions
at stake. To secure this freedom in practice, the editor should have
direct access to the highest level of ownership, not only to a delegated
manager.
Editors of medical journals should have a contract that clearly states
the editor's rights and duties in addition to the general terms of the
appointment and that defines mechanisms for resolving conflict.
An independent editorial advisory board may be useful in helping the
editor establish and maintain editorial policy.

II.B.2. Editorial Freedom

The ICMJE adopts the World Association of Medical Editors' definition
of editorial freedom. This definition states that editorial freedom or
independence is the concept that editors-in-chief should have full
authority over the editorial content of their journal. Journal owners
should not interfere in the evaluation, selection or editing of individual
articles either directly or by creating an environment that strongly
influences decisions. Editors should base decisions on the validity
of the work and its importance to the journal's readers not on the
commercial success of the journal. Editors should be free to express
critical but responsible views about all aspects of medicine without
fear of retribution, even if these views might conflict with the
commercial goals of the publisher. Editors and editors' organizations
have the obligation to support the concept of editorial freedom and
to draw major transgressions of such freedom to the attention of the
international medical, academic, and lay communities.

II.C. Peer Review

Unbiased, independent, critical assessment is an intrinsic part of all
scholarly work, including the scientific process. Peer review is the
critical assessment of manuscripts submitted to journals by experts
who are not part of the editorial staff. Peer review can therefore be
viewed as an important extension of the scientific process. Although
its actual value has been little studied, and is widely debated (4), peer
review helps editors decide which manuscripts are suitable for their
journals, and helps authors and editors in their efforts to improve the
quality of reporting. A peer-reviewed journal is one that submits most
of its published research articles for outside review. The number and
kind of manuscripts sent for review, the number of reviewers, the
reviewing procedures, and the use made of the reviewers' opinions
may vary. In the interests of transparency, each journal should publicly
disclose its policies in its instructions to authors.

II.D. Conflicts of Interest

Public trust in the peer review process and the credibility of published
articles depend in part on how well conflict of interest is handled
during writing, peer review, and editorial decision making. Conflict
of interest exists when an author (or the author's institution), reviewer,
or editor has financial or personal relationships that inappropriately
influence (bias) his or her actions (such relationships are also known
as dual commitments, competing interests, or competing loyalties).
These relationships vary from those with negligible potential to those
with great potential to influence judgment, and not all relationships
represent true conflict of interest. The potential for conflict of interest
can exist whether or not an individual believes that the relationship
affects his or her scientific judgment. Financial relationships (such as
employment, consultantships, stock ownership, honoraria, paid expert
testimony) are the most easily identifiable conflicts of interest and
the most likely to undermine the credibility of the journal, the authors,
and of science itself. However, conflicts can occur for other reasons,
such as personal relationships, academic competition, and intellectual
passion.
All participants in the peer review and publication process must
disclose all relationships that could be viewed as presenting a potential
conflict of interest. Disclosure of these relationships is also important
in connection with editorials and review articles, because it can be
more difficult to detect bias in these types of publications than in
reports of original research. Editors may use information disclosed in
conflict of interest and financial interest statements as a basis for
editorial decisions. Editors should publish this information if they
believe it is important in judging the manuscript.

II.D.1. Potential Conlicts of Interest Related to Individual Authors' Commitments

When authors submit a manuscript, whether an article or a letter, they
are responsible for disclosing all financial and personal relationships
that might bias their work. To prevent ambiguity, authors must state
explicitly whether potential conflicts do or do not exist. Authors should
do so in the manuscript on a conflict of interest notification page that
follows the title page, providing additional detail, if necessary, in a
cover letter that accompanies the manuscript. (See Section II.A.3.
Conflict of Interest Notification Page)
Uniform Requirements

Authors should identify individuals who provide writing assistance and disclose the funding source for this assistance. Investigators must disclose potential conflicts to study participants and state in the manuscript whether they have done so. Editors also need to decide when to publish information disclosed by authors about potential conflicts. If doubt exists, it is best to err on the side of publication.

II.D.2. Potential Conflicts of Interest Related to Project Support

Increasingly, individual studies receive funding from commercial firms, private foundations, and government. The conditions of this funding have the potential to bias and otherwise discredit the research. Scientists have an ethical obligation to submit credible research results for publication. Moreover, as the persons directly responsible for their work, researchers should not enter into agreements that interfere with their access to the data and their ability to analyze it independently, to prepare manuscripts, and to publish them. Authors should describe the role of the study sponsor(s), if any, in study design, in the collection, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the report for publication. If the supporting source had no such involvement, the authors should so state. Biases potentially introduced when sponsors are directly involved in research are analogous to methodological biases of other sorts. Some journals, therefore, choose to include information about the sponsor’s involvement in the methods section.

Editors may request that authors of a study funded by an agency with a proprietary or financial interest in the outcome sign a statement such as, “I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis.” Editors should be encouraged to review copies of the protocol and/or contracts associated with project-specific studies before accepting such studies for publication. Editors may choose not to consider an article if a sponsor has asserted control over the authors’ right to publish.

II.D.3. Potential Conflicts of Interest Related to Commitments of Editors, Journal Staff, or Reviewers

Editors should avoid selecting external peer reviewers with obvious potential conflicts of interest, for example, those who work in the same department or institution as any of the authors. Authors often provide editors with the names of persons they feel should not be asked to review a manuscript because of potential conflicts of interest, usually personal. When possible, authors should be asked to explain or justify their concerns; that information is important to editors in deciding whether to honor such requests.

Reviewers must disclose to editors any conflicts of interest that could bias their opinions of the manuscript, and they should disqualify themselves from reviewing specific manuscripts if they believe it to be appropriate. As in the case of authors, silence on the part of reviewers concerning potential conflicts may mean either that such conflicts exist that they have failed to disclose, or that conflicts do not exist. Reviewers must therefore also be asked to state explicitly whether conflicts do or do not exist. Reviewers must not use knowledge of the work, before its publication, to further their own interests. Editors who make final decisions about manuscripts must have no personal, professional, or financial involvement in any of the issues they might judge. Other members of the editorial staff, if they participate in editorial decisions, must provide editors with a current description of their financial interests (as they might relate to editorial judgments) and disqualify themselves from any decisions where they have a conflict of interest. Editorial staff must not use the information gained through working with manuscripts for private gain. Editors should publish regular disclosure statements about potential conflicts of interests related to the commitments of journal staff.

II.E. Privacy and Confidentiality

II.E.1. Patients and Study Participants

Patients have a right to privacy that should not be infringed without informed consent. Identifying information, including patients' names, initials, or hospital numbers, should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that a patient who is identifiable be shown the manuscript to be published. Authors should identify individuals who provide writing assistance and disclose the funding source for this assistance.

Identifying details should be omitted if they are not essential. Complete anonymity is difficult to achieve; however, and informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of patients is inadequate protection of anonymity. If identifying characteristics are intended to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note. The requirement for informed consent should be included in the journal’s instructions for authors. When informed consent has been obtained it should be indicated in the published article.

II.E.2. Authors and Reviewers

Manuscripts must be reviewed with due respect for authors' confidentiality. In submitting their manuscripts for review, authors entrust editors with the results of their scientific work and creative effort on which their reputation and career may depend. Authors' rights may be violated by disclosure of the confidential details of the review of their manuscript. Reviewers also have rights to confidentiality, which must be respected by the editor. Confidentiality may have to be breached if dishonesty or fraud is alleged but otherwise must be honored.

Editors must not disclose information about manuscripts (including their receipt, content, status in the reviewing process, criticism by reviewers, or ultimate fate) to anyone other than the authors and reviewers. This includes requests to use the materials for legal proceedings.

Editors must make clear to their reviewers that manuscripts sent for review are privileged communications and are the private property of the authors. Therefore, reviewers and members of the editorial staff must respect the authors' rights by not publicly discussing the authors' work or appropriating their ideas before the manuscript is published. Reviewers must not be allowed to make copies of the manuscript for their files and must be prohibited from sharing it with others, except with the permission of the editor. Reviewers should return or destroy copies of manuscripts after submitting reviews. Editors should not keep copies of rejected manuscripts.

Reviewer comments should not be published or otherwise made public without permission of the reviewer, author, and editor.
Uniform Requirements

Opinions differ on whether reviewers should remain anonymous. Authors should consult the information for authors of the journal they have chosen to learn whether the reviews are anonymous. When comments are not signed the reviewers’ identity must not be revealed to the author or anyone else without the reviewer’s permission. Some journals publish reviewers’ comments with the manuscript. No such procedure should be adopted without the consent of the authors and reviewers. However, reviewers’ comments should be sent to other reviewers of the same manuscript, which helps reviewers learn from the review process, and reviewers may be notified of the editor’s decision.

II.F. Protection of Human Subjects and Animals in Research

When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach, and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study. When reporting experiments on animals, authors should be asked to indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

III. Publishing and Editorial Issues Related to Publication in Biomedical Journals

III.A. Obligation to Publish Negative Studies

Editors should consider seriously for publication any carefully done study of an important question, relevant to their readers, whether the results are negative (that is, convincingly allow the null hypothesis to be accepted) or positive (that is, allow the null hypothesis to be rejected). Failure to submit or publish negative studies, in particular, contributes to publication bias. Many studies that purport to be negative are, in fact, inconclusive; publication of inconclusive studies is problematic, since they add little to biomedical knowledge and consume journal resources. The Cochrane Library may be interested in publishing inconclusive trials.

III.B. Corrections, Retractions and "Expressions of Concern"

Editors must assume initially that authors are reporting work based on honest observations. Nevertheless, two types of difficulty may arise. First, errors may be noted in published articles that require the publication of a correction or erratum of part of the work. The corrections should appear on a numbered page, be listed in the contents page, include the complete original citation, and link to the original article and vice versa if online. It is conceivable that an error could be so serious as to vitiate the entire body of the work, but this is unlikely and should be handled by editors and authors on an individual basis. Such an error should not be confused with inadequacies exposed by the emergence of new scientific information in the normal course of research. The latter require no corrections or withdrawals. The second type of difficulty is scientific fraud. If substantial doubts arise about the honesty or integrity of work, either submitted or published, it is the editor’s responsibility to ensure that the question is appropriately pursued, usually by the authors’ sponsoring institution. However, it is not ordinarily the task of editors to conduct a full investigation or to make a determination; that responsibility lies with the institution where the work was done or with the funding agency. The editor should be promptly informed of the final decision, and if a fraudulent paper has been published, the journal must print a retraction. If this method of investigation does not result in a satisfactory conclusion, the editor may choose to conduct his or her own investigation. As an alternative to retraction, the editor may choose to publish an expression of concern about aspects of the conduct or integrity of the work.

The retraction or expression of concern, so labeled, should appear on a numbered page in a prominent section of the print journal as well as in the online version, be listed in the contents page, and include in its heading the title of the original article. It should not simply be a letter to the editor. Ideally, the first author should be the same in the retraction as in the article, although under certain circumstances the editor may accept retractions by other responsible persons. The text of the retraction should explain why the article is being retracted and include a full original citation reference to it.

The validity of previous work by the author of a fraudulent paper cannot be assumed. Editors may ask the author’s institution to assure them of the validity of earlier work published in their journals or to retract it. If this is not done, editors may choose to publish an announcement expressing concern that the validity of previously published work is uncertain.

III.C. Copyright

Many biomedical journals ask authors to transfer copyright to the journal. However, an increasing number of "open access" journals do not require authors to transfer copyright to the journal. Editors should make their position on copyright transfer clear to authors and to others who might be interested in using editorial content from their journals. The copyright status of articles in a given journal can vary: some content cannot be copyrighted (articles written by employees of the U.S. and some other governments in the course of their work, for example), editors may agree to waive copyright on others, still others may be protected under serial rights (that is, use in publications other than journals, including electronic publications, is permitted).

III.D. Overlapping Publications

III.D.1. Duplicate Submission

Most biomedical journals will not consider manuscripts that are simultaneously being considered by other journals. Among the principal considerations that have led to this policy are: 1) the potential for disagreement when two (or more) journals claim the right to publish a manuscript that has been submitted simultaneously to more than one; and 2) the possibility that two or more journals will unknowingly and unnecessarily undertake the work of peer review and editing of the same manuscript, and publish the same article. However, editors of different journals may decide to simultaneously or jointly publish an article if they believe that doing so would be in the best interest of the public’s health.

III.D.2. Redundant Publication

Redundant (or duplicate) publication is publication of a paper that
overlaps substantially with one already published in print or electronic media.

Readers of primary source periodicals, whether print or electronic, deserve to be able to trust that what they are reading is original unless there is a clear statement that the article is being reprinted by the choice of the author and editor. The bases of this position are international copyright laws, ethical conduct, and cost-effective use of resources. Duplicate publication of original research is particularly problematic, since it can result in inadvertent double counting or inappropriate weighting of the results of a single study, which distorts the available evidence.

Most journals do not wish to receive papers on work that has already been reported in large part in a published article or is contained in another paper that has been submitted or accepted for publication elsewhere, in print or in electronic media. This policy does not preclude the journal considering a paper that has been rejected by another journal, or a complete report that follows publication of a preliminary report, such as an abstract or poster displayed at a professional meeting. Nor does it prevent journals considering a paper that has been presented at a scientific meeting but not published in full or that is being considered for publication in a proceedings or similar format. Press reports of scheduled meetings will not usually be regarded as breaches of this rule, but additional data or copies of tables and illustrations should not amplify such reports.

When submitting a paper, the author must always make a full statement to the editor about all submissions and previous reports that might be regarded as redundant or duplicate publication of the same or very similar work. The author must alert the editor if the manuscript includes subjects about which the authors have published a previous report or have submitted a related report to another publication. Any such report must be referred to and referenced in the new paper. Copies of such material should be included with the submitted paper to help the editor decide how to handle the matter.

If redundant or duplicate publication is attempted or occurs without such notification, authors should expect editorial action to be taken. At the least, prompt rejection of the submitted manuscript should be expected. If the editor was not aware of the violations and the article has already been published, then a notice of redundant or duplicate publication will probably be published with or without the author’s explanation or approval.

Preliminary reporting to public media, governmental agencies, or manufacturers, of scientific information described in a paper or a letter to the editor that has been accepted but not yet published violates the policies of many journals. Such reporting may be warranted when the paper or letter describes major therapeutic advances or public health hazards such as severe adverse effects of drugs, vaccines, other biological products, or medicinal devices, or reportable diseases. This reporting should not jeopardize publication, but should be discussed with and agreed upon by the editor in advance.

III.D.3. Acceptable Secondary Publication

Certain types of articles, such as guidelines produced by governmental agencies and professional organizations, may need to reach the widest possible audience. In such instances, editors sometimes choose deliberately to publish material that is also being published in other journals, with the agreement of the authors and the editors of those other journals. Secondary publication for various other reasons, in the same or another language, especially in other countries, is justifiable, and can be beneficial, provided all of the following conditions are met.

1. The authors have received approval from the editors of both journals; the editor concerned with secondary publication must have a photocopy, reprint, or manuscript of the primary version.
2. The priority of the primary publication is respected by a publication interval of at least one week (unless specifically negotiated otherwise by both editors).
3. The paper for secondary publication is intended for a different group of readers, an abbreviated version could be sufficient.
4. The secondary version faithfully reflects the data and interpretations of the primary version.
5. The footnote on the title page of the secondary version informs readers, peers, and documenting agencies that the paper has been published in whole or in part and states the primary reference. A suitable footnote might read: “This article is based on a study first reported in the [title of journal, with full reference].” Permission for such secondary publication should be free of charge.
6. The title of the secondary publication should indicate that it is a secondary publication (complete reproduction, abridged reproduction, complete translation, or abridged translation) of a primary publication. Of note, the National Library of Medicine does not consider translations to be “republications,” and does not cite or index translations when the original article was published in a journal that is indexed in MEDLINE.

III.D.4. Competing Manuscripts Based on the Same Study

Publication of manuscripts to air co-investigators disputes may waste journal space and confuse readers. On the other hand, if editors knowingly publish a manuscript written by only some of a collaborating team, they could be denying the rest of the team their legitimate co-authorship rights; they could also be denying the journal's readers access to legitimate differences of opinion about the interpretation of a study.

Two kinds of competing submissions are considered: submissions by coworkers who disagree on the analysis and interpretation of their study, and submissions by coworkers who disagree on what the facts are and which data should be reported.

Setting aside the unresolved question of ownership of the data, the following general observations may help editors and others dealing with these problems.

III.D.4.a. Differences in Analysis or Interpretation

If the dispute centers on the analysis or interpretation of data, the authors should submit a manuscript that clearly presents both versions. The difference of opinion should be explained in a cover letter. The normal process of peer and editorial review of the manuscript may help the authors to resolve their disagreement regarding analysis or interpretation.

If the dispute cannot be resolved and the study merits publication, both versions should be published. Options include publishing two papers on the same study, or a single paper with two analyses or interpretations. In such cases it would be appropriate for the editor to publish a statement outlining the disagreement and the journal’s involvement in attempts to resolve it.

III.D.4.b. Differences in Reported Methods or Results

If the dispute centers on differing opinions of what was actually done
or observed during the study, the journal editor should refuse publication until the disagreement is resolved. Peer review cannot be expected to resolve such problems. If there are allegations of dishonesty or fraud, editors should inform the appropriate authorities; authors should be notified of an editor’s intention to report a suspicion of research misconduct.

III.D.5. Competing Manuscripts Based on the Same Database

Editors sometimes receive manuscripts from separate research groups that have analyzed the same data set, e.g., from a public database. The manuscripts may differ in their analytic methods, conclusions, or both. Each manuscript should be considered separately. Where interpretations of the same data are very similar, it is reasonable but not necessary for editors to give preference to the manuscript that was received earlier. However, editorial consideration of multiple submissions may be justified in this circumstance, and there may even be a good reason for publishing more than one manuscript because different analytical approaches may be complementary and equally valid.

III.E. Correspondence

Biomedical journals should provide its readership with a mechanism for submitting comments, questions, or criticisms about published articles, as well as brief reports and commentary unrelated to previously published articles. This will likely, but not necessarily, take the form of a correspondence section or column. The authors of articles discussed in correspondence should be given an opportunity to respond, preferably in the same issue in which the original correspondence appears. Authors of correspondence should be asked to declare any competing or conflicting interests.

Public correspondence may be edited for length, grammatical correctness, and journal style. Alternatively, editors may choose to publish correspondence unedited for length or style, as for example in rapid response sections on the Internet, the journal should declare its editorial practice in this regard. Authors should approve editorial changes that alter the substance or tone of a letter or response. Although editors have the prerogative to sift out correspondence material that is irrelevant, uninteresting, or lacking in cogency, they have a responsibility to allow a range of opinion to be expressed. The correspondence section should not be used merely to promote the journal’s, or the editors’, point of view. In all instances, editors must make an effort to screen out discourteous, inane, or libelous statements, and should not allow ad hominem arguments intended to discredit opinions or findings.

In the interests of fairness and to keep correspondence within manageable proportions, journals may want to set time limits for responding to articles and correspondence, and for debate on a given topic. Journals should also decide whether they would notify authors when correspondence bearing on their published work is going to appear in standard or rapid response sections. Journals should also set policy with regard to the archiving of unedited correspondence that appears on line. These policies should be published both in print and electronic versions of the journal.

III.F. Supplements, Theme Issues, and Special Series

Supplements are collections of papers that deal with related issues or topics, are published as a separate issue of the journal or as part of a regular issue, and are usually funded by sources other than the journal’s publisher. Supplements can serve useful purposes: education, exchange of research information, ease of access, focused content, and improved cooperation between academic and corporate entities. Because funding sources can bias the content of supplements through the choice of topics and viewpoints, journals should consider adopting the following principles. These same principles apply to theme issues or special series that have external funding and/or guest editors.

1. The journal editor must take full responsibility for the policies, practices, and content of supplements, including control of the decision to publish all portions of the supplement. Editing by the funding organization should not be permitted.

2. The journal editor must retain the authority to send supplement manuscripts for external peer review and to reject manuscripts submitted for the supplement. These conditions should be made known to authors and external supplement editors before beginning editorial work on the supplement.

3. The journal editor must approve the appointment of any external editor of the supplement and take responsibility for the work of the external editor.

4. The sources of funding for the research, publication, and the products the funding source make that are considered in the supplement should be clearly stated and prominently located in the supplement, preferably on each page. Whenever possible, funding should come from more than one sponsor.

5. Advertising in supplements should follow the same policies as those of the rest of the journal.

6. Journal editors must enable readers to distinguish readily between ordinary editorial pages and supplement pages.

7. Journal editors and supplement editors must not accept personal favors or personal remuneration from sponsors of supplements.

8. Secondary publication in supplements (republication of papers previously published elsewhere) should be clearly identified by the citation of the original paper. Supplements should avoid redundant or duplicate publication. Supplements should not republish research results, but the republication of guidelines or other material in the public interest might be appropriate.

9. The principles of authorship and potential conflict of interest disclosure articulated elsewhere in this document should apply to supplements.

III.G. Electronic Publishing

Most biomedical journals are now published in electronic as well as print versions, and some are published in electronic form only. Electronic publishing (which includes the Internet) is publishing. In the interests of clarity and consistency, the medical and health information published on the Internet should follow the recommendations in this document whenever possible.

The nature of electronic publication requires some special considerations, both within and beyond this document. At a minimum, websites should indicate the following: names, appropriate credentials, affiliations, and relevant conflicts of interest of editors, authors, and contributors; documentation and attribution of references and sources for all content; information about copyright, disclosure of site ownership, and disclosure of sponsorship, advertising, and commercial funding. Linking from one health or medical Internet site to another may be perceived as an implicit recommendation of the quality of the second site. Journals should exercise caution in linking to other sites; when users are linking to another site, it may be helpful to provide an explicit message that they are leaving the journal’s site. If links to
other sites are posted as a result of financial considerations, such
should be clearly indicated. All dates of content posting and updating
should be indicated. In electronic layout as in print, advertising and
promotional messages should not be juxtaposed with editorial content,
and commercial content should be clearly identifiable as such.
Electronic publication is an area that is in flux. Editors should develop,
make available to authors, and implement policies on issues unique
to electronic publishing. These issues include archiving, error correction,
version control, and choice of the electronic or print version of the
journal as the journal of record, publication of ancillary material, and
electronic publication.
In no instance should a journal remove an article from its website
or archive. If an article needs to be corrected or retracted, the written
material must be labeled appropriately and communicated as soon as possible
on a citable page in a subsequent issue of the journal.
Preservation of electronic articles in a permanent archive is essential
for the historical record. Access to the archive should be immediate
and it should be controlled by a third party, such as a library, instead of
of a publisher. Deposition in multiple archives is encouraged.

III. Advertising

Most medical journals carry advertising, which generates income for
their publishers, but advertising must not be allowed to influence
editorial decisions. Journals should have formal, explicit, written
policies for advertising in both print and electronic versions; website
advertising policy should parallel policy for the print version as much
as possible. Editors must have full and final authority for approving
advertisements and enforcing advertising policy.
Where independent bodies for reviewing advertising exist editors
should make use of their judgments. Readers should be able to
distinguish readily between advertising and editorial material. The
juxtaposition of editorial and advertising material on the same products
or subjects should be avoided. Interleaving advertising pages within
articles discourages readers by interrupting the flow of editorial content,
and should be discouraged. Advertising should not be sold on the
condition that it will appear in the same issue as a particular article.
Journals should not be dominated by advertising, but editors should
be careful about publishing advertisements from only one or two
advertisers, as readers may perceive that these advertisers have
influenced the editor.
Journals should not carry advertisements for products that have proved
to be seriously harmful to health—for example, tobacco. Editors should
ensure that existing regulatory or industry standards for advertisements
specific to their country are enforced, or develop their own standards.
The interests of organizations or agencies should not control classified
and other non-display advertising, except where required by law.
Finally, editors should consider all criticisms of advertisements for
publication.

III.1. Medical Journals and the General Media

The public's interest in news of medical research has led the popular
media to compete vigorously to get information about research as
soon as possible. Researchers and institutions sometimes encourage
the reporting of research in the non-medical media before full publication
in a scientific journal by holding a press conference or giving interviews.
The public is entitled to important medical information without
unreasonable delay, and editors have a responsibility to play their part
in this process. Biomedical journals are published primarily for their
readers, but the general public has a legitimate interest in their content;
an appropriate balance should therefore guide journals' interaction
with the media between these complementary interests. Doctors in
practice need to have reports available in full detail before they can
discuss with their patients about the reports' conclusions. Moreover, media
reports of scientific research before the work has been peer reviewed
and fully published may lead to the dissemination of inaccurate or
premature conclusions.
An embargo system has been established in some countries to prevent
publication of stories in the general media before the original paper
on which they are based appears in the journal. The embargo creates
a "level playing field," which most reporters appreciate since it
minimizes the pressure on them to publish stories which they have
not had time to prepare carefully. Consistency in the timing of public
release of biomedical information is also important in minimizing
economic abuses, since some articles contain information that has great
potential to influence financial markets. On the other hand, the embargo
system has been challenged as being self-serving of journals' interests,
and impeding the rapid dissemination of scientific information.
Editors may find the following recommendations useful as they seek
to establish policies on these issues.

• Editors can foster the orderly transmission of medical information
  from researchers, through peer-reviewed journals, to the public. This
  can be accomplished by an agreement with authors that they will not
  publicize their work while their manuscript is under consideration
  or awaiting publication and an agreement with the media that they will
  not release stories before publication in the journal, in return for which
  the journal will cooperate with them in preparing accurate stories.
• Editors need to keep in mind that an embargo system works on
  the honor system; no formal enforcement or policing mechanism
  exists. The decision of any significant number of media outlets, or
  of biomedical journals, not to respect the embargo system would therefore
  lead to its rapid dissolution.
• Very little medical research has such clear and urgent clinical
  implications for the public's health that the news must be
  released before full publication in a journal. In such exceptional
  circumstances, however, appropriate authorities responsible for public
  health should make the decision and should be responsible for the
  advance dissemination of information to physicians and the media. If
  the author and the appropriate authorities wish to have a manuscript
  considered by a particular journal, the editor should be consulted
  before any public release. If editors accept the need for immediate
  release, they should waive their policies limiting prepublication
  publicity.
• Policies designed to limit prepublication publicity should not
  apply to accounts in the media of presentations at scientific meetings
  or to the abstracts from these meetings (see Redundant Publication).
  Researchers who present their work at a scientific meeting should feel
  free to discuss their presentations with reporters, but they should be
discouraged from offering more detail about their study than was
  presented in their talk.
• When an article is soon to be published, editors should help the
  media prepare accurate reports by providing news releases, answering
  questions, supplying advance copies of the journal, or referring reporters
to the appropriate experts. Most responsible reporters find this assistance
should be contingent on the media's cooperation in timing their release
of stories to coincide with the publication of the article.
• Editors, authors, and the media should apply the above stated
  principles to material released early in electronic versions of journals.
III. J. Obligation to Register Clinical Trials

The ICMJE believes that it is important to foster a comprehensive, publicly available database of clinical trials. The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like.

The ICMJE recommends that journals publish the trial registration number at the end of the Abstract. The ICMJE also requires journals to require an online registration for publication in their journals, registration in a public trials registry. The details of this policy are contained under editorials. The ICMJE encourages editors of other biomedical journals to adopt similar policies.

The ICMJE does not advocate one particular registry, but its members will require authors to register their trial in a registry that meets several criteria. The registry must be accessible to the public at no charge. It must be open to all prospective registrants and managed by a not-for-profit organization. There must be a mechanism to ensure the validity of the registration data, and the registry should be electronically searchable. An acceptable registry must include a minimum of the data elements shown in the following table.

<table>
<thead>
<tr>
<th>Item</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Unique trial number</td>
<td>The unique trial number will be established by the primary registering entity (the registry).</td>
</tr>
<tr>
<td>2) Trial registration date</td>
<td>The date of registration will be established by the primary registering entity.</td>
</tr>
<tr>
<td>3) Secondary IDs</td>
<td>May be assigned by sponsors or other interested parties (there may be none).</td>
</tr>
<tr>
<td>4) Funding source(s)</td>
<td>Name of the organization(s) that provided funding for the study.</td>
</tr>
<tr>
<td>5) Primary sponsor</td>
<td>The main entity responsible for performing the research.</td>
</tr>
<tr>
<td>6) Secondary sponsor(s)</td>
<td>The secondary entities, if any, responsible for performing the research.</td>
</tr>
<tr>
<td>7) Responsible contact person</td>
<td>Public contact person for the trial, for patients interested in participating.</td>
</tr>
<tr>
<td>8) Research contact person</td>
<td>Person to contact for scientific inquiries about the trial.</td>
</tr>
<tr>
<td>9) Title of the study</td>
<td>Brief title chosen by the research group (can be omitted if the researchers wish).</td>
</tr>
<tr>
<td>10) Official scientific title of the study</td>
<td>This title must include the name of the intervention, the condition being studied, and the outcome (e.g., The International Study of Digoxin and Death from Congestive Heart Failure).</td>
</tr>
<tr>
<td>11) Research ethics review</td>
<td>Has the study at the time of registration received appropriate ethics committee approval (yes/no)? (It is assumed that all registered trials will be approved by an ethics board before commencing.)</td>
</tr>
</tbody>
</table>

12) Condition

The medical condition being studied (e.g., asthma, myocardial infarction, depression). A description of the study and comparison/control intervention(s) (For a drug or other product registered for public sale anywhere in the world, this is the generic name; for an unregistered drug, the generic name or company serial number is acceptable). The duration of the intervention(s) must be specified.

13) Intervention(s)

Key inclusion and exclusion criteria. Key patient characteristics that determine eligibility for participation in the study. Database should provide drop-down lists for selection. This would include choices for randomized vs. non-randomized, type of masking (e.g., double-blind, single-blind), type of controls (e.g., placebo, active), and group assignment (e.g., parallel, crossover, factorial).

14) Key inclusion and exclusion criteria

Anticipated trial start date

15) Study type

Target sample size

16) Anticipated trial start date

17) Target sample size

18) Recruitment status

19) Primary outcome

20) Key secondary outcomes

*The data fields were specified at a meeting convened by the WHO in April 2005, the explanatory comments are largely from the ICMJE.

IV. Manuscript Preparation and Submission

IVA. Preparing a Manuscript for Submission to a Biomedical Journal

Editors and reviewers spend many hours reading manuscripts, and therefore appreciate receiving with manuscripts that are easy to read and edit. Much of the information in journals’ instructions to authors is designed to accomplish that goal in ways that meet each journal’s particular editorial needs. The guidance that follows provides a general background and rationale for preparing manuscripts for any journal.

IVA 1. General Principles

The text of observational and experimental articles is usually (but not necessarily) divided into sections with the headings Introduction, Methods, Results, and Discussion. This so-called “IMRAD” structure is not simply an arbitrary publication format, but rather a direct reflection of the process of scientific discovery. Long articles may need subheadings within some sections (especially the Results and Discussion sections) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, are likely to need other formats.
Publication in electronic formats has created opportunities for adding details or whole sections in the electronic version only, layering information, cross-linking or extracting portions of articles, and the like. Authors need to work closely with editors in developing or using new publication formats and should submit material for potential supplementary electronic formats for peer review.

Double spacing of all portions of the manuscript—including the title page, abstract, text, acknowledgments, references, individual tables, and legends—and generous margins make it possible for editors and reviewers to edit the text line by line, and add comments and queries, directly on the paper copy. If manuscripts are submitted electronically, the files should be double spaced, because the manuscript may need to be printed out for reviewing and editing.

During the editorial process reviewers and editors frequently need to refer to specific portions of the manuscript, which is difficult unless the pages are numbered. Authors should therefore number all of the pages of the manuscript consecutively, beginning with the title page.

IV.A.1.b. Reporting Guidelines for Specific Study Designs

Research reports frequently omit important information. The general requirements listed in the next section relate to reporting essential elements for all study designs. Authors are encouraged in addition to consult reporting guidelines relevant to their specific research design. For reports of randomized controlled trials authors should refer to the CONSORT statement. This guideline provides a set of recommendations comprising a list of items to report and a patient flow diagram.

Reporting guidelines have also been developed for a number of other study designs that some journals may ask authors to follow (see Table: Reporting Guidelines). Authors should consult the information for journals they have chosen.

### Reporting Guidelines

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Type of study</th>
<th>Source</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSORT</td>
<td>randomized controlled trials</td>
<td><a href="http://www.consort-statements.org">http://www.consort-statements.org</a></td>
<td></td>
</tr>
<tr>
<td>STARD</td>
<td>studies of diagnostic accuracy</td>
<td><a href="http://www.consort-statements.org/stardstatement.htm">http://www.consort-statements.org/stardstatement.htm</a></td>
<td></td>
</tr>
<tr>
<td>QUOROM</td>
<td>systematic reviews and meta-analyses</td>
<td>[<a href="http://www.consort-statements.org/initiatives/">http://www.consort-statements.org/initiatives/</a> MOOSE/mOOSE.pdf](<a href="http://www.consort-statements.org/initiatives/">http://www.consort-statements.org/initiatives/</a> MOOSE/mOOSE.pdf)</td>
<td></td>
</tr>
<tr>
<td>STROBE</td>
<td>observational studies in epidemiology</td>
<td><a href="http://www.strobe-statements.org">http://www.strobe-statements.org</a></td>
<td></td>
</tr>
<tr>
<td>MOOSE</td>
<td>meta-analyses of observational studies in epidemiology</td>
<td>[<a href="http://www.consort-statements.org/initiatives/">http://www.consort-statements.org/initiatives/</a> MOOSE/mOOSE.pdf](<a href="http://www.consort-statements.org/initiatives/">http://www.consort-statements.org/initiatives/</a> MOOSE/mOOSE.pdf)</td>
<td></td>
</tr>
</tbody>
</table>

### IV.A.2. Title Page

The title page should carry the following information:

1. The title of the article. Concise titles are easier to read than long, convoluted ones. Titles that are too short may, however, lack important information, such as study design (which is particularly important in identifying randomized controlled trials). Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.
2. Authors’ names and institutional affiliations. Some journals
3. The name of the department(s) and institution(s) to which the work should be attributed.
4. Disclaimers, if any.
5. Corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript; (the "corresponding author"); this author may or may not be the "guarantor" for the integrity of the study as a whole, if someone is identified in that role. The corresponding author should indicate clearly whether his or her e-mail address is to be published.
6. The name and address of the author to whom requests for reprints should be addressed or a statement that reprints will not be available from the authors.
7. Source(s) of support in the form of grants, equipment, drugs, or all of these.
8. A running head. Some journals request a short running head or foot line, usually of no more than 40 characters (count letters and spaces) at the foot of the title page. Running heads are published in most journals, but are also sometimes used within the editorial office for filing and locating manuscripts.
9. Word counts. A word count for the text only (excluding abstract, acknowledgments, figure legends, and references) allows editors and reviewers to assess whether the information contained in the paper warrants the amount of space devoted to it, and whether the submitted manuscript fits within the journal's word limits. A separate word count for the Abstract is also useful for the same reason.
10. The number of figures and tables. It is difficult for editorial staff and reviewers to tell if the figures and tables that should have accompanied a manuscript were actually included unless the numbers of figures and tables that belong to the manuscript are noted on the title page.

### IV.A.3. Conflict of Interest Notification Page

To prevent the information on potential conflict of interest for authors from being overlooked or misplaced, it is necessary for that information to be part of the manuscript. It should therefore also be included on a separate page or pages immediately following the title page. However, individual journals may differ in where they ask authors to provide this information and some journals do not send information on conflicts of interest to reviewers. (See Section II.D. Conflicts of Interest)

### IV.A.4. Abstract and Key Words

An abstract (requirements for length and structured format vary by journal) should follow the title page. The abstract should provide the context or background for the study and should state the study's purposes, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations.

Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to be careful that abstracts reflect the content of the article accurately. Unfortunately, many abstracts disagree with the text of the article (6). The format required for structured abstracts differs from journal to journal, and some journals use more than one structure; authors should make it a point to prepare their abstracts in the format specified by the journal they have chosen.
Some journals request that, following the abstract, authors provide, and identify as such, 3 to 10 key words or short phrases that capture the main topics of the article. These will assist indexers in cross-indexing the article and may be published with the abstract. Terms from the Medical Subject Headings (MeSH) list of Index Medicus should be used; if suitable MeSH terms are not yet available for recently introduced terms, present terms may be used.

IVA.5. Introduction

Provide a context or background for the study (i.e., the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation; the research objective is often more sharply focused when stated as a question. Both the main and secondary objectives should be made clear, and any pre-specified subgroup analyses should be described. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

IVA.6. Methods

The Methods section should include only information that was available at the time the plan or protocol for the study was written; all information obtained during the conduct of the study belongs in the Results section.

IVA.6.a. Selection and Description of Participants

Describe your selection of the observational or experimental participants (patients or laboratory animals, including controls) clearly, including eligibility and exclusion criteria and a description of the source population. Because the relevance of such variables as age and sex to the object of research is not always clear, authors should explain their use when they are included in a study report; for example, authors should explain why only subjects of certain ages were included or why women were excluded. The guiding principle should be clarity about how and why a study was done in a particular way. When authors use variables such as race or ethnicity, they should define how they measured the variables and justify their relevance.

IVA.6.b. Technical information

Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well known; describe new or substantially modified methods, give reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration. Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

IVA.6.c. Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as the use of P values, which fails to convey important information about effect size. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the computer software used.

IVA.7. Results

Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Extra or supplementary materials and technical detail can be placed in an appendix where it will be accessible but will not interrupt the flow of the text; alternatively, it can be published only in the electronic version of the journal. When data are summarized in the Results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Restrict tables and figures to those needed to explain the argument of the paper and to assess its support. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid non-technical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."

Where scientifically appropriate, analyses of the data by variables such as age and sex should be included.

IVA.8. Discussion

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or the Results section. For experimental studies it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice. Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, authors should avoid making statements on economic benefits and costs unless their manuscript includes the appropriate economic data and analyses. Avoid claiming priority and alluding to work that has not been completed. State new hypotheses when warranted, but clearly label them as such.

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IVA.9.a. General Considerations Related to References

Although references to review articles can be an efficient way of guiding readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible. On the other hand, extensive lists of references to original work on a topic can use excessive space on the printed page. Small numbers...
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